UNIVERSITY OF SOUTHAMPTON

FACULTY OF HEALTH SCIENCES

The prevalence and natural history of radiographic foot osteoarthritis and co-existing foot pain in a UK population-based cohort of older women.

By

Peter McQueen

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Thesis submitted for the degree of Master of Philosophy & MPhil candidature

Foreword

UNIVERSITY OF SOUTHAMPTON,

ABSTRACT

FACULTY OF HEALTH SCIENCES

Doctor of Philosophy

'THE PREVALENCE AND NATURAL HISTORY OF RADIOGRAPHIC FOOT OSTEOARTHRITIS AND CO-EXISTING FOOT PAIN IN A UK POPULATION-BASED COHORT OF OLDER WOMEN' by Peter McQueen

Introduction The prevalence of foot osteoarthritis (OA) is less well understood than hip, knee and hand OA. The foot is undoubtedly more complex, and investigators have been challenged in defining which joints to investigate and by the need for improved methodological standardisation across studies. As such, the prevalence and natural history of osteoarthritis and the relevance of co-existing pain in the foot have not yet been widely explored. The aim of this thesis was to improve understanding of foot osteoarthritis by examining techniques used to define foot osteoarthritis and by description of the prevalence, distribution and natural history of radiographic foot osteoarthritis and co-existing foot pain in an established UK population-based cohort of women, 'The Chingford 1000 Women Study'.

Methods

Study 1: The author (PMc) undertook training by an experienced radiographer in scoring foot osteoarthritis using a validated foot atlas (The La Trobe Foot Atlas). Employing archived foot radiographs (n = 20 paired feet) Chingford 1000 Women study: year 6, 1995) intra-rater reliability was established for five individual joints in both feet (percentage close agreement ranged from 47.6% to 85.7% for osteophytes and from 33.3% to 81% for joint space narrowing). Subsequently a sample of foot radiographs (n=218) that included all remaining participants in the Chingford 1000 Women Study who returned for the year '23' visit (mean (SD) for age: 75.5 (5.1)) were scored. A range of prevalence estimates of osteoarthritis at the foot and individual joint level were examined that relate to discordance between different techniques of interpretation. The findings from this study supported the use of the La Trobe Foot Atlas (LFA) to identify foot osteoarthritis in existing current and historical radiographs of established large population cohorts.

Study 2: A cross-sectional study design was used in which returning participants at year '23' (2013-2015) from the Chingford 1000 Women study were investigated for presence of radiographic foot osteoarthritis and co-existing foot pain. Presence of radiographic foot osteoarthritis was scored according to LFA and self-reported foot pain was primarily defined and assessed using the non-side specific question "have you ever had pain in your feet which has lasted one day or longer?"

Data from 332 women were included in this study. Of these 91.3% had radiographic foot osteoarthritis in any joint affecting either foot. When examining individual joints, the rank order of radiographic osteoarthritis was; 2nd cuneo-metatarsal joint (78.9%), 1st cuneo-metatarsal joint

(57.8%), 1st metatarsophalangeal joint (51.8%), navicular1stcuneiform joint (30.3%) and tarsonavicular joint (28.4%). 30.5% (n=96) reported ever having foot pain and 20.5% reported having current foot pain. The prevalence of symptomatic (foot pain plus foot OA) foot osteoarthritis was 20.8% (n=192).

Study 3: A longitudinal, 17-year cohort design was used in which the presence of radiographic foot osteoarthritis and foot pain at the first metatarsophalangeal joint (1stMTPJ) was investigated in participants at year 6 (1995) and year '23' (2013-2015) from the Chingford 1000 Women study. Descriptive analysis was conducted using only participants for whom complete data sets for pain and radiographic foot data were available at both time points. Data from 197 women were included in this study. Of these, co-existence of radiographic foot osteoarthritis of the 1st MTPJ and foot pain was higher at year '23' (incidence: 12.7% left foot and 17.9% right foot). Participants (n=192) who had radiographic foot osteoarthritis and foot pain at year 6 had higher level of foot pain at year '23' compared to participants who did not have foot pain at year 6.

Conclusion The findings from this MPhil support the use of the LFA to identify foot osteoarthritis in existing current and historical radiographs to improve methodological standardisation across future investigations. The findings that a high prevalence of radiographic foot osteoarthritis exists among older women, but only 1 in 4 of these have symptomatic radiographic foot osteoarthritis contributes to an understanding of the range of prevalence estimates of foot osteoarthritis that currently exists within the published literature. The reporting of incidence for progression of osteoarthritis at the first metatarsophalangeal joint (1st MTPJ) over a 17-year period is a novel contribution to the field. This MPhil thesis work supports the call for a focus on a global consensus for defining foot OA beyond the 1st MTPJ to provide a clear definition for use in existing and future population cohorts and in clinical trials for foot OA.

Thesis word count: 60,589

Foreword

DEDICATION

I wish to dedicate this thesis to my sister Mrs Rachel K Carlisle BMus (Hons) MA ATCL PGCE (Cantab) who was most deserving of a PhD award but did not have the same privileged support that I received.

"I did this for the both of us."

LIST OF CONTENTS

Contents

Chapter 1: Introduction 1
1.0. Introductory chapter summary 1
1.1. Background 1
1.2. Aim of the MPhil 3
1.2.1. General aim and scope of the MPhil thesis 3
1.3 Context of the MPhil project within the funded program of research 3
1.4 MPhil Study populations 4
1.5. Unique contribution to the ELFOAB project by the MPhil student 5
1.6. Summary 7
Chapter 2: Literature review and Background 8
2.0. Introductory chapter summary 8
2.1. Introduction 8
2.2. Literature search strategy and results 9
2.2.1. Epidemiology 9
2.3. Structural osteoarthritis 10
2.3.1. Pathophysiology 10
2.3.2. Osteophytes 10
2.3.3. Joint space narrowing 11
2.4. Diagnosis of osteoarthritis 12
2.5. Identification of structural osteoarthritis 12
2.6. Structural foot osteoarthritis 15
2.7. Measurement of joint disease involvement: Foot osteoarthritis atlas 16
2.8. Management of foot osteoarthritis and context of wellbeing 18
2.9. Foot Pain 19
2.10. Foot Joint Pain (Arthralgia) 21
2.11. Co-existence of radiographic foot osteoarthritis and foot pain 24
2.12. Pathophysiology of bone marrow oedema and its relevance to arthralgia 25
2.13. Natural history of radiographic osteoarthritis and foot pain 26
2.14. Literature review findings 27
2.14.1. Summary of the evidence gap 27
2.14.2. Research Questions; 28
2.14.3. Aims and objectives of study 1, 2 and 3 investigations (Chapters 4, 5 & 6) 28
2.14.3.1. Study 1 (Chapter 4) 28
2.14.3.2. Study 2 (Chapter 5) 29
2.14.3.3. Study 3 (Chapter 6) 29

2.15. Summary 29
Chapter 3: Chingford 1000 women study 30
3.0. Introductory chapter summary 30
3.1. Study design 30
3.2. Study participants 30
3.3. Study sample size of return study participants 31
3.4. Data selection and participant recruitment 31
3.5. Governance 33
3.5.1. Ethical committee approval 33
3.5.2. Data handling and storage 33
3.5.3. Patient risks and avoidance measures 33
3.6. Radiographic scoring of participant images 35
3.7. Training undertaken by the Podiatrist for carrying out radiographic scoring 39
3.8. Inclusion and exclusion criteria 40
3.9. Chingford 1000 Women study data collection environment and timescale 43
3.10. Summary 43
Chapter 4: Study 1 – Feasibility in scoring radiographic foot osteoarthritis using the LFA 44
4.0. Introductory chapter summary 44
4.1. Introduction 44
4.2. Study aims and objectives 46
4.3. Methods 46
4.3.1. Study Design 46
4.3.2. Study 1 (Chapter 4) Justification of methods: Feasibility in scoring radiographic foot osteoarthritis using the LFA 46
4.3.3. Study participants (foot radiographs) 51
4.3.4. Data collection for intra-rater reliability of scoring foot radiographs 52
4.3.5. Data collection for scoring foot radiographs to test technique appropriateness 53
4.3.6. Radiographic scoring method for foot osteoarthritis 53
4.3.7. Scoring technique using the LFA to determine radiographic foot osteoarthritis 54
4.3.7.1 Intra-rater reliability: Scoring technique 54
4.3.7.2 Validity and appropriateness: Scoring technique 54
4.3.8. Statistics 56
4.4. Results 58
4.4.1. Intra-rater reliability (year 6, technique 1) 58
4.4.1.1. Intra-rater reliability in determining presence of foot osteoarthritis using the LFA, technique 1 58
4.4.1.2. Intra-rater reliability in determining presence of individual foot joint osteoarthritis using the LFA, technique 1. 59

4.4.2. Appropriateness (year '23'; comparison of techniques 1 and 2) 61
4.4.2.1. Technique 1 compared to technique 2 (ungradable joints as missing) 61
4.4.2.2. Technique 1 compared to Technique 3 (over-scoring) 63
4.4.3. Validity of the scoring method between the two radiographic views (dorsoplantar and lateral) 65
4.4.3.1. Technique 2: Foot osteoarthritis according to dorsoplantar, lateral and combined projections 65
4.4.3.2. Technique 3: Foot osteoarthritis according to dorsoplantar, lateral and combined projections 66
4.4.4. Prevalence of radiographic osteoarthritis 67
4.4.4.1. Prevalence of radiographic osteoarthritis scores in the dorsoplantar projection 67
4.4.4.2. Prevalence of radiographic osteoarthritis scores in the lateral projection 68
4.5. Summary of findings 70
4.5.1. Intra-rater reliability 70
4.5.2. Appropriateness 70
4.5.3. Validity 70
4.6. Discussion 71
4.6.1. Intra-rater reliability 71
4.6.2. Appropriateness 73
4.6.3. Validity 74
4.7. Strengths and potential limitations 75
4.8. Conclusion 77
4.8.1 Key Points 77
4.8.2 Summary 78
Chapter 5: Study 2 – Prevalence of radiographic foot osteoarthritis and foot pain 79
5.0. Introductory chapter summary 79
5.1. Introduction 79
5.2. Study aims and objectives 81
5.3. Methods 81
5.3.1. Participant recruitment 81
5.3.2. Data Collection 81
5.3.3. Location 82
5.3.4. Study design 82
5.3.5. Assessment of demographic and clinical characteristics 85
5.3.6. Assessment of radiographic foot osteoarthritis 86
5.3.7. Assessment of foot pain 87
5.3.8. Assessment of disabling foot pain 93
5.3.9. Assessment of the co-existence of radiographic osteoarthritis and foot pain, and disabling foot pain 95

5.3.10. Revisions to foot pain manikin variables for shading of foot pain (year '23') 95
5.4. Statistical Analysis 98
5.4.1. Descriptive population characteristics 98
5.4.2. Sample size calculation 99
5.5. Results 99
5.5.1. Response rate 100
5.5.2. Participant demographic 100
5.5.3. Prevalence of osteoarthritis 102
5.5.3.1. Prevalence of radiographic osteoarthritis by osteophytic change and joint space narrowing and by individual joint 105
5.5.3.2. Prevalence of rOA stratified according to age and painful rOA according to age 107
5.5.3.3. Prevalence of foot rOA stratified according to Body Mass Index (BMI), and painful foot rOA with BMI 109
5.6. Prevalence of foot pain 111
5.6.1. Generalised Foot Pain - ever experienced foot pain lasting one day or longer (MFPDI Foot manikin) 112
5.6.2. Generalised Foot Pain – Foot pain in the past month lasting one day or longer (MFPDI Foot manikin) 113
5.6.3. Global Foot Pain 115
5.6.3.1. Global Foot Pain using Disabling foot pain measures 117
5.6.3.2. Prevalence of Global Foot Pain stratified according to age 118
5.6.3.3. Prevalence of Global Foot Pain stratified according to BMI 120
5.6.4 Foot Joint Pain: Clinician diagnosed foot pain 123
5.7. Presence of radiographic foot osteoarthritis and co-existing pain 124
5.7.1. Additional co-existing Global Foot Pain: Disabling foot pain 125
5.8. Summary of results 126
5.8.1. Description of the prevalence of radiographic foot osteoarthritis 126
5.8.2. Description of the prevalence of foot pain 126
5.8.3. Analysis of the relationship between radiographic foot osteoarthritis and foot pain 126
5.9. Discussion 126
5.9.1 Prevalence of radiographic foot osteoarthritis 127
5.9.2. Prevalence of foot pain 129
5.9.2.1. Generalised Foot Pain (Gen.FP) 129
5.9.2.2. Global Foot Pain 131
5.9.2.3. Foot Joint Pain: Clinician diagnosed foot pain 133
5.9.3. Radiographic foot osteoarthritis and co-existing pain 134
5.9.4. Strengths and potential limitations 136
5.10. Conclusion 138
5.10.1. Key Points 138

5.10.2. Summary 139
Chapter 6: Study 3: The natural history of radiographic foot osteoarthritis and co-existing foot pain UK among a cohort of older women 140
6.0. Introductory chapter summary 140
6.1. Introduction 140
6.2. Aims and objectives 142
6.3. Methods 142
6.3.1. Study Design 142
6.3.1.0. Participant recruitment 143
6.3.1.1. Timescale 143
6.3.1.3. Sample size 144
6.3.2. Data collection 145
6.3.2.0. Assessment of radiographic foot osteoarthritis for longitudinal analysis. 145
6.3.2.1. Procedure for identifying radiographic foot OA 148
6.3.2.2. Assessment of radiographic foot osteoarthritis 148
6.3.2.3. Assessment of foot pain 148
6.4. Statistical analysis 149
6.5. Results 151
6.5.1. Response rate 152
6.5.2 Participant demographics 152
6.5.3 Prevalence of person level radiographic (polyarticular evaluated) foot osteoarthritis 152
6.5.4 Prevalence of joint specific radiographic foot OA at year 6 and year '23' 153
6.5.5 Natural history of radiographic 1st metatarsophalangeal joint osteoarthritis 154
6.5.6 Changes of radiographic 1st MTPJ OA from year 6 to year '23' 154
6.5.7 The natural history of developing symptomatic radiographic foot OA 156
6.6. Summary of results 157
6.6.1. Paired sample characteristics 157
6.6.2. Prevalence of radiographic foot OA and of foot pain at year 6 157
6.6.3. Analysis of the change in prevalence of radiographic foot OA from year 6 to year '23' 157
6.6.4. Analysis of the natural history of developing symptomatic radiographic foot OA 158
6.7. Discussion 158
6.7.1. Background demographics at study baseline, x-ray baseline and x-ray follow-up 159
6.7.2. Natural history 159
6.7.2.1. Natural history of radiographic osteoarthritis of the foot 159
6.7.2.2. Natural history of pain in the foot 160
6.7.2.3. Natural history of radiographic osteoarthritis of the 1st MTPJ 160
6.7.2.4. Natural history of asymptomatic radiographic osteoarthritis of 1st MTPJ at year 6 relative to presence of foot pain at year '23' 162

6.7.3. Strengths and potential limitations....163
6.8. Conclusion....168
6.8.1. Key Points....168
6.8.2. Summary....168
Chapter 7 Discussion....170
7.0. Introductory chapter summary....170
7.1. Introduction....170
7.2. Radiographic scoring technique for foot osteoarthritis....171
7.3. The prevalence of radiographic foot osteoarthritis and co-existing foot pain....172
7.4. The natural history of radiographic foot osteoarthritis and co-existing foot pain....173
7.5. Critique of research methodologies....174
7.5.1. Acknowledged limitations....174
7.5.2. Strengths of the study....177
7.5.3. Participant samples....179
7.5.4. Radiographic imaging technique....179
7.5.5. Radiographic evaluation of osteoarthritis....180
7.5.6. Definition of foot pain....181
7.6. Future work....182
7.6.1. Implications for clinical practice....182
7.6.2. Implications for future research....183
7.7. Conclusions....185
Appendix 1 LFA....187
Appendix 1 Australi....187
Appendix 2 Example search strategy using PICO chart for literature review (Cluett 2005)....208
Appendix 3 Example Flow chart of results of literature review presented....210
Appendix 4 Pain definitions....211
Appendix 5 Consent form for C1000W study....214
Appendix 6 Study protocol for study....215
Appendix 7 Ethical approval for C1000W study....216
Appendix 8 MFPDI....217
Appendix 9 Possible bias introduced into research....218
Appendix 10 Manchester Foot Pain and Disability Index 17 (MFPDI)....223
Appendix 11 Prevalence of osteoarthritis stratified according to grading in the dorsoplantar view....225
Appendix 12 Prevalence of osteoarthritis stratified according to grading in the lateral view....226
Appendix 13 Impact on results from the limitation of differing x-ray methods....228
Appendix 14 IMFAA incorporated into Chingford questionnaires....229
Appendix 15 La Trobe Foot Atlas limitations....232

Appendix 16 Core measures of data collection for the benefit of future research 234
10.0 References 235

LIST OF TABLES

Table 1 Comparison between definitions of individual grades 17
Table 2: Pain assessments within the literature 24
Table 3 Images of dorsoplantar and lateral projections used 36
Table 4 Inclusion and Exclusion criteria 41
Table 5 Feasibility explored 47
Table 6 Kappa scores and corresponding definitions 50
Table 7 Scoring disparity between techniques whilst using the LFA 56
Table 8 Agreement of the presence of foot osteoarthritis in either left or right feet 59
Table 9 Agreement of diagnosis according to radiographic feature in each joint 60
Table 10 Prevalence of radiographic osteoarthritis according to five joints and radiographic view according to technique 1 and technique 2 (ungradables as missing) 62
Table 11 Prevalence of radiographic osteoarthritis according to five joints and radiographic projection showing differences between technique 1 and technique 3 (overscoring). 64
Table 12 Prevalence of osteoarthritis stratified according to grading in the dorsoplantar view (N=218) 69
Table 13 Prevalence of osteoarthritis stratified according to grading in the lateral view (N=218) .. 69
Table 14 Core variables including in clinical data collection 86
Table 15 Pain questions in questionnaires 90
Table 16 Types of Disabling Foot Pain from literature 95
Table 17 Number of pain diagrams completed according to versions of questionnaires 96
Table 18 Demographic & clinical variables – Descriptive statistics – year '23' 100
Table 19 year '23' demographical characteristics of participants 101
Table 20 Demographic comparison between responders and non-responders at radiographical visit for year '23' 101
Table 21 Distribution summary of participants with any presence of radiographic osteoarthritis at joint, foot and feet level (N=218) 102
Table 22 Joint assessment ranking order 104
Table 23 Prevalence in rank order by radiographic feature 106
Table 24 Radiographic foot joint osteoarthritis stratified according to age N=215 107
Table 25 Radiographic foot joint osteoarthritis stratified according to BMI N=217 109
Table 26 Prevalence of having ever experienced foot pain lasting one day or longer (N=315) 112
Table 27 Prevalence of having experienced foot pain in the past month lasting one day or longer (N=315) 113

Table 28 Cross tabulation of participants foot pain experience in the past month or ever 114
Table 29 Manchester Foot Pain and Disability Index 17 (MFPDI) response frequencies of Australian populations and a UK population-based cohort of women (NWAHS (W) N=135; NWASHS (Yrs) N=57; C1000W N=118) 115
Table 30 Global Foot Pain (shaded MFPDI foot pain manikin) stratified according to age N=312 118
Table 31 Global foot pain (shaded MFPDI foot pain manikin) stratified according to BMI (N=313).. 120
Table 32 Current foot joint pain diagnosed by passive joint motion by a clinician 123
Table 33 Demographic & clinical characteristics: year 6 & '23' 152
Table 34 Prevalence of radiographic osteoarthritis at year 6 and of year '23' among participants who attended both x-ray visits 152
Table 35 Prevalence of change from year 6 to year '23' among paired participants 153
Table 36 Prevalence of year 6 and year '23' paired sample in the 1st metatarsophalangeal joint (1st MTPJ) 154
Table 37 Natural history of 1st MTPJ radiographic osteoarthritis 154
Table 38 changes in radiographic score for the 1st MTPJ between year 6 and year '23'. 155
Table 39 Prevalence of foot pain at year 6 and year '23' 156
Table 40 Progression of asymptomatic radiographic osteoarthritis at year 6 to symptomatic radiographic osteoarthritis at year '23'. 156
Table 41 Natural history: Baseline foot radiographic osteoarthritis with co-existing presence of foot pain and co-existing foot pain at follow-up 156
Table 42 Prevalence of foot pain at (Year '23) with presence and absence of radiographic OA at year 6. 157

LIST OF FIGURES

Figure 1 ELFOAB project 4
Figure 2 Key areas of identification and the respective characteristics of osteoarthritis 15
Figure 3 Flow diagram of successive data collection points in the Chingford 1000 women study 34
Figure 4 Radiographic foot image showing dorsoplantar projection joints in LFA (taken from year '23' x-rays) 37
Figure 5 Radiographic foot image showing lateral projection joints evaluated in LFA (taken from year '23' radiographs). 37
Figure 6 Diagnosis of multifaceted radiographic foot osteoarthritis in multiple projections 39
Figure 7 Intra-rater reliability procedure 52
Figure 8 Validity and appropriateness of technique procedure 52

Figure 9 Foot radiograph highlighting disparity between techniques 56
Figure 10 Summary of the foot x-ray protocol at year '23' 83
Figure 11 Full body manikin 88
Figure 12 Global pain with reference to the feet 89
Figure 13 MFPDI foot pain diagram - Plantar aspect 91
Figure 14 MFPDI foot pain diagram - Dorsal aspect 91
Figure 15 Otter et al. (2010) demarcated foot pain diagram - dorsal aspect 97
Figure 16 Otter et al. (2010) demarcated foot pain diagram - plantar aspect 97
Figure 17 Global foot pain: Self-reported foot pain on most days in the last three months (marked with shading) N=197* 116
Figure 18 Diagnosis of multifaceted radiographic foot osteoarthritis in multiple projections 146
Figure 19 Diagnosis of radiographic knee osteoarthritis 147
Figure 20 Diagnosis of radiographic single joint osteoarthritis in a single projection 147
Figure 21 Natural history summarised: Prevalence of radiographic osteoarthritis presence with and without foot pain at baseline showing those who present with pain at follow-up 150
Figure 22 Natural history summarised: Prevalence of participants with and without radiographic osteoarthritis at baseline who present with foot pain at follow-up 150

LIST OF GRAPHS

Graph 1 Summary of radiographic osteoarthritis by foot in each joint 103
Graph 2 Prevalence of osteophytic change and joint space narrowing according to each joint 105
Graph 3 Differing definitions to establish disabling foot pain 117
Graph 4 Prevalence of foot pain and co-existing radiographic foot osteoarthritis 124
Graph 5 Differing definitions to establish disabling foot pain 125

DECLARATION OF AUTHORSHIP

This thesis has been undertaken as part of the PhD full time academic programme with the Faculty of Health Sciences at the University of Southampton.

The MPhil is embedded within a larger programme of research; Epidemiology and Lifetime Risk of Foot Osteoarthritis and Biomechanics (ELFOAB). The ELFOAB research proposal was led and conceived by Professor Catherine Bowen, Professor Nigel Arden and Professor Michael Doherty who sought funding support from the Dr William M Scholl Research and Development Fund.

I was the lead researcher and principal investigator, with input from the supervisory team, for the first phase of the ELFOAB project, which investigated the epidemiology of foot osteoarthritis and co-existing foot pain in a UK population-based cohort of older women. For data collection, I was responsible for clinical foot assessments and acquiring and scoring of all foot x-rays as well as data cleaning, data analysis and data management. Radiographic imaging was conducted by the ELFOAB study radiographers (InHealth and Holly House Hospital) and participant recruitment, background demography and general health assessments were conducted by the ELFOB clinical research assistants. I undertook all write-up activities. The thesis was professionally proof-read for typographical and grammatical errors, inconsistencies and errors of sentence or phrase composition initially by Mrs Bryony Graves BSc and later by Ruth Arundell BA (hons) MA PGCE CELTA.

I, Peter McQueen declare that this thesis entitled:

'The prevalence and natural history of radiographic foot osteoarthritis and co-existing foot pain in a UK population-based cohort of older women.'

and all related work within this thesis are my own and have been produced as a result of the research I have carried out. All other sources of information included within the thesis have been acknowledged.

The following can be confirmed:

- This work was done wholly or mainly while in candidature for a research degree at this university;
- Where any part of this thesis has previously been submitted for a degree or any other qualification at this University of any other institution, this has been clearly stated;
- Where I have consulted the published work of others, this is always clearly attributed;
- Where I have quoted from the work of others, the source is always given. With exception of quotation, this thesis is entirely my own work;
- I have acknowledged all main sources of help;
- Where the thesis is based on work done by myself jointly with others, I have made clear exactly what was done by others and what I have contributed myself;
- Parts of this work have been presented or published. The publication of material primarily relates to Chapter 5 and is listed in the publications section on page xxi.

Signed:

Date: 4/12/2019

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LIST OF ABBREVATIONS

BMI – Body Mass Index

C1000W – Chingford 1000 Women study

CASF – Clinical Assessment of Study of the Foot

CMJ – cuneo-metatarsal joint

ELFOAB – Epidemiology and lifetime risk of osteoarthritis within the foot and biomechanical functional outcomes

FHSQ – Foot Health Status Questionnaire

FJP – Foot Joint Pain

GenFP – Generalised Foot Pain

GFP – Global Foot Pain

IPJ – interphalangeal joint

IRAS – Integrated Research Application System

JSN – Joint Space Narrowing

K - Kappa

LFA – La Trobe Foot Atlas

MFPDI – Manchester Foot Pain and Disability Index

MRI – Magnetic Resonance Imaging

MSK – musculoskeletal

MTPJ – metatarsophalangeal joint

N1stCJ – navicular 1st cuneiform joint

NHS – National Health Service

OA – osteoarthritis

OP – osteophyte

Foreword

P – Probability

PA – percentage agreement

PPI – Patient and Public Involvement

rOA – radiographic osteoarthritis

rOA+ – positive diagnosis of radiographic osteoarthritis

rOA- – negative diagnosis of radiographic osteoarthritis

ROM – Range of Motion

SE – Standard Error

SMC – Silverthorn Medical Centre (formerly Chingford Hospital)

SOP – Standard Operating Procedures

TNJ – talonavicular joint

ABBREVIATED NAMES

CB – Catherine Bowen

LG – Lucy Gates

MD – Michael Doherty

MM – Michelle Marshall

NA – Nigel Arden

PMc – Peter McQueen

PUBLICATIONS, PRESENTATIONS AND AWARDS

The publications, presentations and awards listed below, were as a result of the work involved in the Doctor of Philosophy;

Publications:

- Adams J, Woods-Townsend K, Grace M, Warner M, Bowen C, McQueen P, Dando C and Stokes M (2015) **Raising teenagers' awareness of musculoskeletal health through LIFELAB: A collaboration between school students, teachers and clinical academic researchers.** *Rheumatology* 54 (S1): i37.
- McQueen P, Gates L, Marshall M, Doherty M, Arden N and Bowen C (2017) **Interpretation of radiographic grading of foot osteoarthritis in older women: The Chingford general population cohort.** *Journal of Foot and Ankle Research* 10:54.

Awards:

- Dr William M. Scholl Podiatric Research and Development Endowment Fund PhD studentship awarded to P. L. McQueen

Conference presentations

- McQueen PL, Bowen CJ**,** Daniels M, Cherry L, Doherty M, Arden NK. (2013) **Radiographical abnormality of hallucal sesamoids in middle-aged females.** *The Society of chiropodists and Podiatrists Annual Conference*.
- McQueen Pl, Bowen CJ, Daniels M, Doherty M, Arden NK (2013) **Protocol: Epidemiology & lifetime risk of osteoarthritis in the foot.** *Arthritis Research UK Centre for Sport, Exercise and Osteoarthritis; Annual conference.*
- McQueen Pl, Bowen CJ, Daniels M, Doherty M, Arden NK (2014). **Orthoses: The honest problem with patient success when proving the value of key podiatric treatment.** *The Society of chiropodists and Podiatrists Annual Conference.*
- Adams J, Woods - Townsend K, Grace M, Warner M, Bowen C, McQueen P, Dando C, Stokes M. (2015) **Raising teenagers' awareness of musculoskeletal health through LIFELAB: A collaboration between school students, teachers and clinical academic researchers**. *Rheumatology* 54(S1): i37
- McQueen PL (2014) **Osteoarthritis and foot joint pain**. *Arthritis Research UK Centre for Sport, Exercise and Osteoarthritis; Annual conference; Risk Factors focus*

- McQueen PL (2014) **ELFOA - Epidemiological study: Relationship between foot osteoarthritis and foot joint pain.** *Arthritis Research UK Centre for Sport, Exercise and Osteoarthritis; Risk Factors Theme Day*
- McQueen Pl, Bowen CJ, Daniels M, Doherty M, Arden NK (2015). **Painful foot osteoarthritis: a common symptom in a common pathology?** *The Society of chiropodists and Podiatrists Annual Conference.*

Other presentations:

- McQueen PL, Bowen CJ**,** Gates L (2013) **Project update; The Epidemiology and Lifetime Risk of Foot Osteoarthritis and Associated Lower Limb Biomechanical Factors**. *SOLLAR strategy meeting*
- McQueen PL (2015) **Three Minute Thesis: Foot osteoarthritis; The silent joint crippler**. *Three minute thesis*

Chapter 1: Introduction

1.0. Introductory chapter summary

This chapter provides background and context to the MPhil project in terms of the current research and healthcare provision for foot pain and foot osteoarthritis. The general aims of the thesis are identified, and the study population is discussed. Finally, the unique contribution of the MPhil student and related ownership within the MPhil project are defined.

1.1. Background

Foot pain arising from foot osteoarthritis (OA) is a debilitating condition which is poorly understood but is a common occurrence among the general population (Roddy et al. 2015). Research of other joints diagnosed with OA has demonstrated a likely effect on the quality of life of those living with the condition (Imamura et al. 2008). With an increase in the aging population and an obesity epidemic, it is expected that the prevalence of symptomatic osteoarthritis will increase, such that the demand for care provision may also increase (Zhang and Jordan 2010).

Despite an increase in understanding of the epidemiology, aetiology and pathology of knee, hip and hand osteoarthritis, the presence of osteoarthritis occurring in the foot remains to be explored in detail. Furthermore, there is a need for future research to focus on a global consensus when defining foot osteoarthritis, and to research beyond the historically limited scope of the 1stMTPJ. An example of the consequence of the disparity in the current research is the issuing of orthoses to patients, where the effect on osteoarthritic joints, whether positive or negative, remains to be established despite recent investigations in this area (Sena da Conceição et al. 2015; Halstead et al. 2016).

It is possible that this discordance is due to the heterogeneity between authors when defining radiographic and symptomatic foot osteoarthritis (Roddy et al. 2015), and a lack of methodological standardisation across studies (Trivedi et al. 2010). Evidence of this can be observed in governmental clinical guidance documents on osteoarthritis, which have provided limited clarification of these issues, and refer to unconvincing definitions of osteoarthritis (NICE 2014).

Although research exists on foot osteoarthritis in people with foot symptoms (Roddy et al. 2015), few research studies have examined the prevalence of radiographic foot osteoarthritis, beyond the 1st MTPJ. Furthermore, few studies have recruited from a general population to investigate the presence of foot osteoarthritis irrespective of a diagnosis of pain.

Investigation of osteoarthritis at other joint sites has enabled consideration of associations between structural change and pain which, at best, have a weak association (Zhang and Jordan 2010). However, Hadler (1992) considered a novel perspective in understanding osteoarthritis within the context of pain. Hadler stated that knee pain, rather than the presence of osteoarthritis, is the 'malady', thereby inferring that the focus of research should be reconsidered, and also alluded to professionals often assuming a relationship whereby the process of structural change in osteoarthritis is reflective of the pain experience. Hadler (1992) illustrated this concept by describing the clinical management pathway of a typical patient presenting with knee pain being followed up with the observation of osteophytic change using radiographic imaging.

These novel perspectives challenge the current attitudes in the treatment and management of osteoarthritis. In summary of the concept described by Hadler, traditionally the focus has been primarily on understanding and developing knowledge of structural osteoarthritis irrespective of pain involvement. However, Hadler (1992) explored a new perspective in understanding the epidemiology of osteoarthritis through a more empathetic approach towards patients. This understanding challenged the focus on structural osteoarthritis to make pain the primary focus of investigation with respect to its clinical significance as a patient concern (Zhang and Jordan 2008).

In addition to the limited research on foot osteoarthritis and foot pain in the measurement of the effectiveness of the current management of osteoarthritis, foot healthcare outcomes have received little consideration (Halstead et al. 2016). However, preliminary research of the treatment benefit of specialist podiatric care to patients with musculoskeletal disorders, has more recently been considered. Rome et al. (2013) demonstrated a significant difference in patient reported outcomes with podiatric intervention using a newly formed service in New Zealand. The research is basic in terms of its methodology in identifying the disease, pathological complaint and treatment specific reduction in foot pain. However, the research highlights the need for and value of podiatric care among those in the general population who are suffering with musculoskeletal conditions. Whilst research relating to managing foot conditions has increased, that investigating foot osteoarthritis remains limited. Most available evidence relates to chronic conditions such as diabetes (Formosa et al. 2016), rheumatoid arthritis (Hennessy et al. 2016) and, more recently, long term management of chronic conditions (Edwards et al. 2016). Recent advances have improved the understanding of mechanisms of the aetiology of osteoarthritis within the foot and ankle (Zhang 2010). The foot is undoubtedly complex, and investigators have been challenged in defining which specific joints to

focus on, and with improving methodological standardisation across studies. As such, the prevalence and natural history of osteoarthritis and the relevance of co-existing pain in the foot have not yet been explored in extensive or detailed terms.

1.2. Aim of the MPhil

1.2.1. General aim and scope of the MPhil thesis

The aim of this thesis was to improve understanding of foot osteoarthritis by examining techniques used to define foot osteoarthritis. This was fulfilled through the description of the prevalence, distribution and natural history of radiographic foot osteoarthritis and co-existing foot pain in an established UK population-based cohort of women, 'The Chingford 1000 Women Study'.

The work was carried out in three phases:
(1) To establish a reliable technique for scoring of foot radiographs for presence of radiographic foot OA.
(2) To describe the cross-sectional prevalence of radiographic foot osteoarthritis and foot pain in a UK population-based cohort of older women.
(3) To describe the natural history of radiographic foot osteoarthritis at the 1st metatarsophalangeal joint and foot pain in a UK population-based cohort of older women.

1.3 Context of the MPhil project within the funded program of research

This MPhil project is embedded within a larger programme of research, the Epidemiology and Lifetime Risk of Osteoarthritis and Biomechanics project (ELFOAB). The project is funded by the Dr William M Scholl Podiatric Research and Development Fund. The research was designed as a multi-centre project involving the universities of Southampton, Nottingham, Oxford and East London. Figure 1 presents the role of each centre for the ELFOAB programme of work.

The aim of the ELFOAB programme is;
'to develop a detailed understanding of the prevalence, risk factors and associations of osteoarthritis occurring within the feet in a UK population-based cohort of older women at middle and older age. An additional aim is to determine lower limb biomechanical factors associated with radiographic foot osteoarthritis.'

Study 1 of the ELFOAB programme is entirely fulfilled by this MPhil thesis work as a standalone project. Data collection and analysis from this study then led to the completion of ELFOAB studies 2

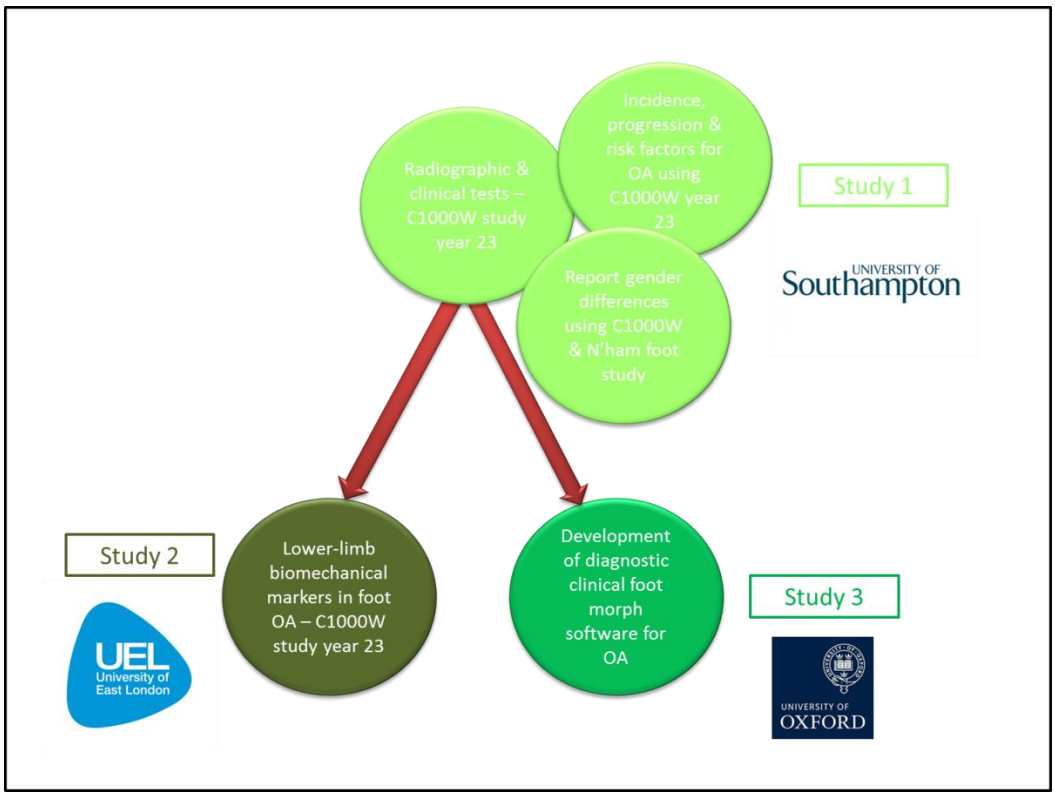
and 3 by researchers at the University of East London and the University of Oxford respectively (Figure 1).

1.4 MPhil Study populations

The study population that forms the basis for this MPhil thesis work is the Chingford 1000 Women study (chingfordstudy.org.uk) currently led by one of the supervisory team, Professor Nigel Arden.

The Chingford 1000 Women Study was originally set up in June 1989 as a retrospective case control study and evolved to become a prospective longitudinal population-based cohort study by Dr Deborah Hart and Professor Tim Spectre, St Thomas Hospital, London to investigate osteoporosis and in subsequent years, osteoarthritis.

Figure 1 ELFOAB project



**Consistent input has been contributed by the University of Nottingham which was also in part the source of recruitment of participants into study 1.*

The Chingford 1000 women study began in 1989 to study osteoporosis. The focus later shifted to the investigation of osteoarthritis of the knee, hip and hand. As the study was set up as a prospective cohort study, many variables were collected throughout the 25 year term of the study. Although

radiographic imaging was carried out in the feet (year 6), no analysis was carried out until 2012 when inter-rater reliability of diagnosing foot osteoarthritis was first considered using the La Trobe Foot Atlas (LFA) (Merriman et al. 2012). Evidence of foot pain has also been collected from the study participants and was reviewed for the first time in 2014 by the ELFOAB study principal investigator, Professor Catherine Bowen (Gay et al. 2014).

1.5. Unique contribution to the ELFOAB project by the MPhil student

The thesis author (PMc) was the first to consider the prevalence and natural history of radiographic foot osteoarthritis with the co-existence of foot pain. As the lead researcher, with input from the supervisory team, this MPhil thesis investigates, for the first phase of the ELFOAB project, the epidemiology of foot osteoarthritis and co-existing foot pain in a UK population-based cohort of older women. The author's involvement as lead researcher for the returning final phase of the Chingford 1000 Women Study enabled, for the first time, 17-year longitudinal data to be examined.

The Chingford year '23' foot study was considered within the ELFOAB study for NHS ethics approval in May 2013. As lead researcher for this returning cohort, the thesis author (PMc) was responsible for liaising with the diagnostic imaging leads (including the respective NHS radiology service and private hospital) across different sites, being responsible for overseeing the quality of the Chingford study year '23' radiographic imaging. The latter involved the writing and setting up of standard operating procedures for the standardisation of images.

A review of the literature was carried out which facilitated refinement of the research questions and informed the necessary additional variables required for the thesis, both of which were developed by the thesis author with the support of the supervisory team. The initial research question developed by the ELFOAB project included the identification of risk factors affecting the progression of radiographic foot osteoarthritis and also gender differences in radiographic foot osteoarthritis and reported foot characteristics. It was revealed, through the review of literature, that understanding of radiographic foot osteoarthritis is underdeveloped. It was therefore agreed with the supervisory team that the initial project outline to investigate radiographic foot osteoarthritis was ambitious and unrealistic within the given MPhil timeframe.

There was considerable challenge in defining radiographic foot osteoarthritis using a tested and validated scoring atlas which had little to no global consensus prior to the development of the thesis. As it was clear that scoring technique could differ substantially depending on the interpretation style

of the atlas user, the thesis author sought to identify interpretation techniques and to consider the best technique to serve as the case definition for the thesis. Further to this, the definition of foot pain was also found to lack global consensus in research literature, and yet the quantity of available tested and validated variables were by no means limited. The numerous available variables were collected using one study population and demonstrated the respective prevalence data in the interest of establishing a case definition which would also benefit the thesis. This work was developed by and solely completed by the thesis author and was not only a key contribution to the thesis structure but also has implications for the future body of research.

All changes in the project proposal were completed by the thesis author who then submitted an ethics application (IRAS) for a substantial amendment which included additional foot pain items within questionnaires, and changes to the radiographic projections of the diagnostic foot imaging in order to answer the thesis research question. These amendments can be understood through the version changes outlined in Chapter 3. All changes made to the questionnaires and x-ray protocol by the thesis author were presented to and agreed by the supervisory team with the corresponding changes to the ethics application subsequently being made by the thesis author.

The thesis author carried out all foot related data collection with the Chingford 1000 Women Study returning cohort (N=332) with the exception of the x-ray imaging. However, all radiographic data used in the thesis were generated through scoring by the thesis author for the presence and extent of radiographic osteoarthritis in the foot. Data collection took place over a twenty-month period and required the thesis author to travel weekly to the main research site in North East London, Chingford for data collection of the clinical variables. An online data entry and management programme was co-developed by the thesis author and a statistics manager based at the University of Oxford with the purpose of streamlining and simplifying the data entry of Chingford year '23' (Research Electronic Data Capture software REDCap) (Harris et al. 2009). Although data entry of Chingford questionnaires was carried out by a junior research assistant, scored data for the x-rays were entered into an Excel database by the thesis author (estimated data entry for over 12,500 joints).

As part of the dissemination activities, the thesis author wrote an extract about the proposed foot study for the Chingford newsletter in order to provide an update to participants. The thesis author also assisted in the organisation of the 25th anniversary tea-party in July 2017 to thank participants for their continued participation in and support for the study. Finally, throughout the MPhil thesis investigations, presentations of the research proposal (specific to the MPhil project) and interim

analyses of data were presented in various formats to the College of Podiatry, Arthritis Research UK, University of Southampton three-minute thesis (3MT) faculty heat (2015) and the University of Oxford epidemiology osteoarthritis research focus group.

1.6. Summary

The MPhil thesis and respective investigations were conceived from a larger programme of work that aimed to explore the epidemiology and biomechanics of foot OA. The investigations presented in this thesis constitute the work of the thesis author, with input from the supervisory team. The following chapters fulfil a need for research in radiographic osteoarthritis. The chapters are summarised as follows:

Chapter 2 provides a detailed review of the literature relevant to the key themes of this work with a focus on justification for the investigation of radiographic foot osteoarthritis and co-existing foot pain.

Chapter 3 provides a comprehensive description of the Chingford 1000 Women Study returning participants' recruitment and methods employed in each of the three investigations.

Chapter 4 describes the results of the evaluation of the thesis author's reliability in scoring foot osteoarthritis as well as examination of different interpretive techniques in scoring that may affect the prevalence estimates for foot OA.

Chapter 5 describes the results of the cross-sectional and descriptive component of the study including prevalence of foot OA, prevalence of foot pain and prevalence of foot osteoarthritis with co-existing foot pain in a UK population-based cohort of older women.

Chapter 6 describes the results of the longitudinal analysis of prevalence of foot OA, prevalence of foot pain and prevalence of foot osteoarthritis with co-existing foot pain in a UK population-based cohort of older women.

Chapter 7 discusses and brings together the findings of the investigations of Chapters 4, 5 and 6 in the context of the available literature, study limitations, clinical implications and suggestions for future work.

Chapter 2: Literature review and Background

2.0. Introductory chapter summary

Chapter 1 provided a context and preliminary justification of the thesis, identifying the challenges of research in rheumatology specific to foot osteoarthritis and foot pain. A brief explanation of where the proposed research would be positioned within the current body of research was provided and the aim of the thesis was outlined. This chapter is a review of the literature which informs the research aims and objectives of the three studies which fulfil the aim of the thesis as described in chapter 1. The defined study aims and objectives lead to a description of the established study used to fulfil the study aims.

2.1. Introduction

The review of literature explores the following areas; pathophysiology of osteoarthritis and associated joint features, diagnosis and identification of osteoarthritis, management of osteoarthritis, foot pain, natural history of co-existing foot osteoarthritis and foot pain, and a summary of findings.

Key to this chapter was the preceding work which shaped and formed the literature review and thus informed the final research question (section 2.14.2). This work involved extensive consideration of search terms and a strategy (Appendix 2) which was limited but crucial in directing the methodology, study design and research question, with the aim of producing work that would contribute to the current pool of research without duplicating previous research activity. This thesis is based upon careful consideration of a relevant body of literature, and aims to provide a basis on which the limitations of the existing literature can be addressed. Critically, global consensus among research groups was a key issue relating to the measurement of both foot pain and foot osteoarthritis in previous research studies and fundamental aspects of epidemiology in this area were considerably limited by the availability of longitudinal data.

The overarching aim of the MPhil project has been formed through thorough exploration of the literature whilst recognising the need to produce higher quality research in a complex and under researched area of the body.

The effect of disability resulting from foot osteoarthritis is largely unknown in terms of the effect on the general population and on the healthcare economy (Thomas et al. 2004). However, estimates of

one in six people being affected by symptomatic foot osteoarthritis suggest a possible societal impact resulting from the disease (Roddy et al. 2015).

2.2. Literature search strategy and results

Review of the literature was based on search strategies which are detailed in Appendix 2. Search strategies were carried out to consider rOA and co-existing foot pain guided by the PICO structure. However, the tightly focused search terms resulted in a limited number of articles identified. This was indicative of the availability of research in this area. As a result, searches were additionally run on radiographic foot osteoarthritis and on foot pain to provide more extensive review of the literature and greater depth to the discussion. Literature search databases included Medline, Embase and CINAHL.

Through searching for literature relevant to the thesis, it was evident when eliminating articles by title and content that literature documenting the effectiveness of treatments and interventions in foot osteoarthritis was readily available. However, basic descriptive work outlining epidemiology of the disease as the foundational knowledge required in order to generate research on the management of osteoarthritis was limited. Additionally, it became evident that hip and knee osteoarthritis were advanced in terms of epidemiology (including established, standardised and validated diagnostic methods) which had enabled the subsequent research regarding the management of osteoarthritis.

The review of literature explores fundamental concepts in the background of structural foot osteoarthritis, of foot pain, and of their co-existence whilst also considering the identification of or diagnostic approaches to these. Finally, in the interests of fulfilling a comprehensive review of key concepts recognised within epidemiology, the natural history of osteoarthritis and co-existing pain was considered at other sites, as this was not considered within the foot prior to this thesis being created.

2.2.1. Epidemiology

Epidemiology is considered to relate primarily to the distribution and determinants of disease (Silman & Macfarlane 2002). Information about this can then be used to form strategies both for the prevention and management of the disease (Fernandes et al. 2013). Epidemiology is the most appropriate research approach for this project as it will identify the scale of the problem in terms of

quantifying population prevalence and will also identify the clinically significant groups which require more focused research in the future.

2.3. Structural osteoarthritis

2.3.1. Pathophysiology

Osteoarthritis is considered to be the most prevalent joint disorder in the world and is identified using either joint symptoms or structural changes, or by incorporating both features (Arden and Nevitt 2006). Key characteristics of osteoarthritis include osteophytic formation, the development of osseus projections at the joint and joint space narrowing where the cartilage becomes thinner. Arden (2006) describes the disease as comprising focal damage, cartilage loss, abnormal remodelling, subarticular bone attrition, osteophytes, ligamentous laxity, muscle weakness (peri-articular) and less commonly synovial distension and inflammation. Zhang and Jordan (2008) describe the disease as being recognisable through pathological, radiographic or clinical presentation in the context of epidemiology. These authors expand the definition of radiographic osteoarthritis using the Kellgren and Lawrence grading system of osteophytes, joint space narrowing and the 'presumed' appearance of sclerosis, cysts and deformity in severe grades. Key symptoms in osteoarthritis are considered to include joint pain and stiffness whilst dysfunction is also considered, but with lesser significance (Kean 2004).

Due to the complexity of the disease, the multi-pathological nature of osteoarthritis lends itself to the recently considered concept of "joint failure", the common phenotype seen in an osteoarthritic joint (Brandt 2008). Felson and Neogi (2004) expand on the recently developed understanding of joint pathology as being a 'whole organ disease'. They state that it occurs as a consequence of pathological abnormality existing in periarticular muscles, ligaments, synovium, the neurosensory system and bone. Brandt et al. (2008) describe the aetiopathology as the failed repair of damage caused by the mechanical stresses exerted on the joint tissues. The authors explain the occurrence of overwhelming mechanical abnormality through the body's inability to be effective in its reparative processes within the context of a joint.

2.3.2. Osteophytes

Osteophytes are generally accepted as 'fibrocartilage-capped bony outgrowths originating in the periosteum'. There are two subcategories of osteophyte; those contained within the insertion of tendons and ligaments known as 'traction spurs', and syndesmophytic change in the insertion of ligaments and tendons which are known as 'inflammatory spurs' (often visible in patients with ankylosing spondylitis). However, the most commonly encountered osteophyte is the

osteochondrophyte (often referred to simply as 'osteophyte') which develops in the periosteum at the junction between bone and cartilage (van der Kraan and Van der Berg 2007). It is the latter osteophyte that is of particular relevance to the pathological presentation of osteoarthritis. It involves the process of osteophytosis, where new bone forms at the joint margins. The cells in developing osteophytes go through the process of chondrogenesis, and osteoblasts replace the matured hypertrophic chondrocytes (Zuscik et al. 2008). This process results in the bony outgrowths which are visible through diagnostic imaging (Junker et al. 2016). The purpose of these structural changes is unknown, however, it has been suggested that in larger joints (hip and knee), due to the association between recovery of the joint space and the development of large osteophytes, the purpose may be in stabilising the joint (Doherty et al. 2002). However, it is known that the subchondral bone, periosteum, synovium, ligaments, and the joint capsule are all innervated, with the capacity to initiate the pain pathway (Dieppe and Lohmander 2005).

2.3.3. Joint space narrowing

Diarthrodial (or synovial) joints consist of two bone ends with cartilaginous end plates contained within a soft membrane of synovium containing synovial fluid (Allan 1998). The hyaline cartilage (synovium) is a low-friction material which can accommodate weight by distributing it across a joint surface whilst being a wear-resistant tissue (Pearle et al. 2005). The synovium is a highly metabolically active structure containing synoviocyte cells, purposed with the nourishment of chondrocytes, and the removal of metabolites and biproducts of matrix destruction (Seren and Barenbaum 2010). It is recognised that several mechanisms result in the degradation of the articular cartilage, bone remodelling and inflammation of the synovium on a molecular level (Dieppe & Lohmander 2005). The extracellular matrix contains the articular structure which is comprised of collagen and aggrecan which deteriorate (Dieppe and Lohmander et al. 2005). As cartilage is considered to be aneural, it is therefore unlikely to be responsible for any pain effected within the joint region (Dieppe & Lohmander 2005). It must therefore be deduced that the source of pain is from other structures irrespective of any association between pain and structural change of the cartilage.

2.4. Diagnosis of osteoarthritis

Flores and Hochberg (2003) discuss five key areas in the identification of osteoarthritis;

- Clinical
- Histological
- Pathological
- Biomechanical
- Biochemical

A clinical diagnosis of osteoarthritis includes the following characteristics; joint pain, tenderness, limitation of movement, crepitus, occasional effusion and variable degrees of local inflammation (Figure 2) (Flores and Hochberg 2003). These clinical characteristics generally have a poor association with structural changes in foot osteoarthritis and are under-researched within the literature. As symptoms of osteoarthritis have traditionally been the primary reason for patient contact in the clinical setting, it is inevitable that pain should be considered as the primary focus of studies on osteoarthritis. Pain is also considered by Hunter et al. (2008) to be the predominant symptom in patients. Yet it is the measured pathological characteristics (Figure 2) that can most effectively provide an objective diagnosis of osteoarthritis and these will be explored in greater detail.

2.5. Identification of structural osteoarthritis

The Gold-standard diagnostic pathway for identification and classification of osteoarthritis is through histological analysis using biopsy samples (Sellam & Barenbaum 2010). However, in live participants, this approach would be neither ethical nor appropriate. Diagnostic imaging provides the means to evaluate a joint with a non-invasive approach and therefore minimal risk to the patient. The Gold-standard for diagnostic imaging is using magnetic resonance as this captures the greatest level of detail (inclusive of soft tissues; articular cartilage, synovium, menisci, intra-articular structures and intra-osseus changes). This is more consistent with current philosophical understanding whereby a joint is considered to be an organ (Peterfy & Kothari 2006). Magnetic Resonance imaging also ensures that techniques can easily be repeated, unlike radiographic images which require a series of images (Peterfy & Kothari 2006).

However, conventional radiography is the primary imaging modality documented in current research studies which provides a means to validated semiquantitative measures used to evaluate osteoarthritis in the foot. In terms of the Magnetic Resonance Imaging (MRI) (which is more inclusive of soft tissues) there is a distinct lack of research available, with the first conclusive scoring system

having been published in 2017 by Halstead et al. It is evident that MRI has become more established in research as an emerging imaging modality in other sites including the hip and knee. However, the foot continues to be under-researched in bone pathogenesis specific to the basic structural changes of osteophytic change and joint space narrowing in foot osteoarthritis (Guermazi et al. 2013). Radiographic imaging can effectively measure these changes and, within the clinical setting, provides an inexpensive and fast diagnostic method enabling a body of evidence to be developed efficiently, which reflects the research in other sites (Guermazi et al. 2009). Among population studies, it is also recognised that MRI is a technique which is more logistically challenging as a result of the greater demand on resources (Dieppe & Lohmander 2005). In addition, although approaches using radiographic imaging may be perceived to be disadvantaged by the inability to capture cartilaginous tissue (unlike MRI which can effectively capture cartilage tissue), the joint space width between bony structures provides a measure of cartilaginous change. Furthermore, joint space width measurements in the knee have been demonstrated as comparable to the cartilage morphology in MRI derived images when investigating progression of osteoarthritis (Duryea et al. (2010). This demonstrates that although MRI may be more inclusive of all joint structures, conventional radiographic imaging has an important role, particularly in the early stages of research into osteoarthritis, with no disadvantage to the key characteristics evaluated on x-ray.

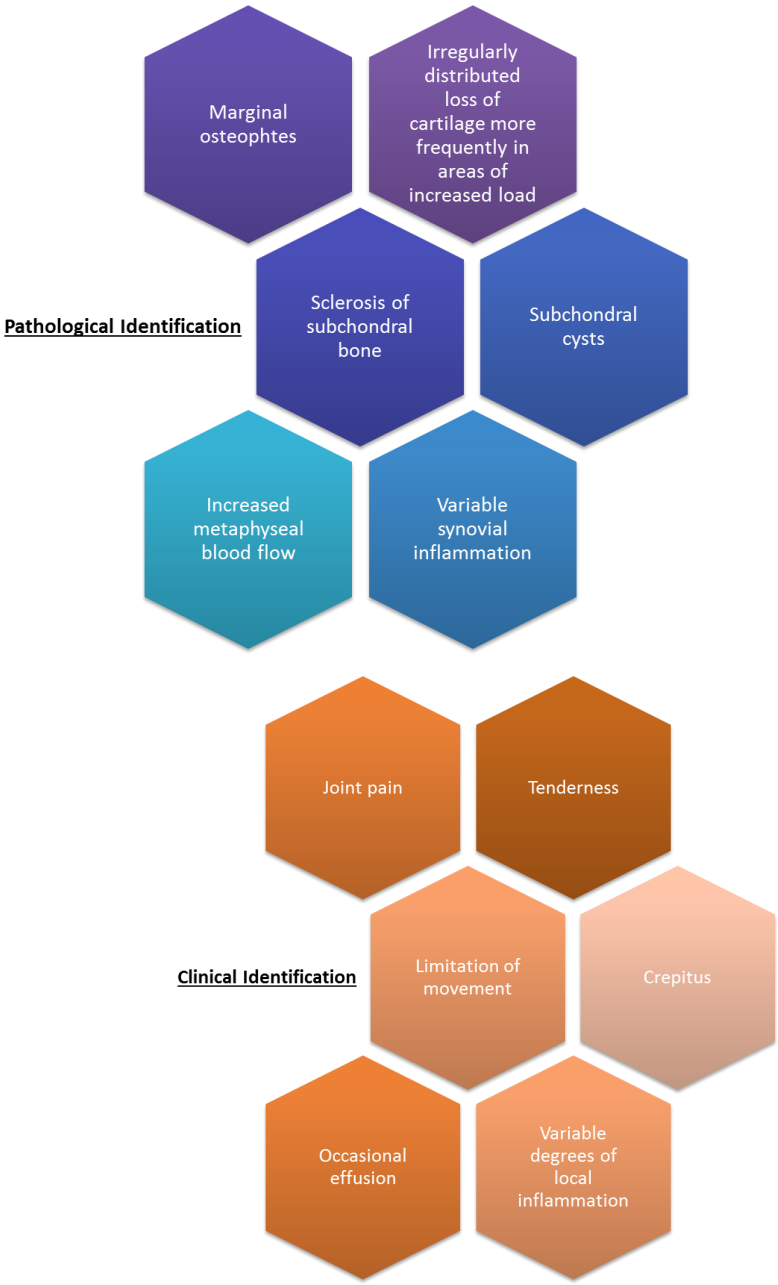
Trivedi et al. (2010) reviewed the literature to establish 27 relevant research articles on foot related radiographic imaging where 19 articles made use of the Kellgren and Lawrence system for diagnosing osteoarthritis. The authors also found three studies using the LFA which had been published three years earlier. The remaining five articles used radiographic characteristics in combination; number of osteophytic protrusions, cartilage thickness (using ossified surfaces as reference points) and osteophytes. However, the latter characteristics were omitted when investigating the foot (having been originally included for the hip, knee and ankle). MRI was not used as an imaging modality by any research group, which be due to the logistical challenges and the availability of validated measurement tools, as only two tools were widely used and they were specific to radiographic assessments. It is of note that the Kellgren and Lawrence (1958) atlas was not developed for use with the foot, and this lack of specificity inevitably impacts on its validity and reliability when applied to the foot joints. For this reason, the LFA represents a more relevant and appropriate tool for evaluating osteoarthritic change in the foot.

The most commonly used radiographic characteristics are osteophytes and joint space narrowing (Trivedi et al. 2010; Arden and Nevitt 2006; Abhishek 2013). Brandt et al. (2008) discuss that where

emphasis is placed on one characteristic of osteoarthritis, in particular, joint space narrowing, it is a misguided perspective given the involvement of all joint tissues. Importantly however, the Kellgren and Lawrence (1958) atlas and the LFA (Menz et al. 2007) consider two pathological characteristics (osteophytes and joint space narrowing). Radiographic imaging modality may not be reflective of the current understanding of joints as organs where all tissues are affected by disease (see 2.4). However, the use of MRI on patients may be inappropriate to a degree. The justification for not using MRI should be considered, in part due to the potential influencing bias or subjectivity of other soft tissue characteristics affected by osteoarthritis. These characteristics cannot be distinguished using conventional radiographic images and are therefore less likely to influence the observer when focusing on the two radiographic features. Most importantly, there is also no availability of validated and reliable foot atlases that would be required for MRI (Menz et al. 2009). These interpretative elements, on the part of the investigator, may be difficult to eliminate as a bias even where a conscious effort has been made to avoid the issue. This would therefore hypothetically result in a likely over-estimation of osteoarthritis when compared to other studies. It can therefore be deduced that conventional radiography is the most appropriate method of diagnosis of osteoarthritis in the foot at this stage of epidemiological research.

Radiographic definition was found to be the most employed criteria used to establish a diagnosis of osteoarthritis in a systematic review whereby 58% of studies used this as the primary outcome measure (Pereira et al. 2011). A narrative review by Hunter and Guermazi (2012) highlighted the insensitivity to early changes in joints due to osteoarthritis but also accepted the cost efficiency and widespread use of radiographic definition as a measure in epidemiological studies. Conversely, Xu et al. (2013) have made the discovery that in hip osteoarthritis, radiographic imaging is more sensitive than MRI when assessing bone attrition, osteophytic change, and diffuse cartilage damage but poor sensitivity exists in diagnostic imaging of subchondral cysts.

Figure 2 Key areas of identification and the respective characteristics of osteoarthritis



2.6. Structural foot osteoarthritis

Pereira et al. (2011) defined osteoarthritis as a disease involving the synovial joints in which 'focal' loss occurs within the articular cartilage alongside hypertrophy of the bone (osteophytic changes and subchondral bone sclerosis) and thickening of the capsule.

A recent change in current thinking on osteoarthritis makes the case that osteoarthritis is not simply limited to the concept of *"wear and tear"*. However, the challenge remains to discard this general understanding among sufferers and health and medical professionals. The need to reconsider this dated understanding is also recognised by Hadler (1992) who mentions osteoarthritis as consisting of a subset of joint disorders. Hadler (1992) alludes to osteoarthritis being a multifactorial disease with the resultant shared common pathological features (or 'phenotype') as later denoted by (Doherty 2001).

Of note, Menz et al. (2009) established a combined joint prevalence of 39.4% osteoarthritis within the foot. Wilder et al. (2005) however, found a site specific prevalence of 20% foot osteoarthritis among men and women using the Kellgren and Lawrence tool (1958) in the Clearwater Osteoarthritis Study, a prospective cohort consisting of over 3500 participants. In a systematic review of the literature, Trivedi et al. 2010) concluded that the literature available on foot osteoarthritis focussed mainly on the 1st metatarsophalangeal joint and that population based studies needed to be pursued in order to quantify the prevalence of osteoarthritis among different joint complexes and to effectively define osteoarthritis subtypes within the foot.

2.7. Measurement of joint disease involvement: Foot osteoarthritis atlas

The LFA is based on the atlas (appendix 1) produced by Kellgren and Lawrence (1958) for grading radiographic imaging of osteoarthritis. The atlas includes an additional view to use as an alternative in identifying joint condition where it is not possible in the primary view. The atlas utilises a zero to three scoring system for osteophytic changes and changes in joint space narrowing. The continued use of the Kellgren and Lawrence tool for over half a century is testament to its appropriateness for its intended purpose of establishing the extent of disease involvement in a joint. However, the atlas was developed for use with hip, knee and hand joints and few tools have considered joints in the foot. Notably, research is well documented in osteoarthritis of the knee (Down et al. 2011; Neumann et al. 2009; Metcalfe et al. 2012), hip (Parimi et al. 2010; Ganz et al. 2008) spine and hands (Kortekaas et al. 2011), however, the foot is often overlooked. This distinct lack of research in osteoarthritis within the foot was recognised by Wilder et al. (2005) and is likely influenced by the availability of atlases.

The LFA was developed for the study by Menz et al. (2007) to aid identification of osteoarthritis specific to the foot and considers five medial joints; first metatarsophalangeal joint (1st MTPJ), first and second cuneo-metatarsal joint (CMJ), navicular first cuneiform joint (N1stCNJ) and the talonavicular joint (TNJ). As such, the only alternative atlas available prior to the development of the

LFA was the Kellgren and Lawrence scoring method which is limited by its specificity to other joints in the body (interphalangeal hand joints, carpometacarpal joints, wrist, spine, hips and knees). The justification provided by the authors on their choice of joints was due to the ability to examine a joint in both lateral and dorsoplantar projections and based on the authors' experience as the joints most frequently affected by osteoarthritis. It could be speculated that the difficulty in identifying and assessing more anatomically lateral foot joints in the lateral projection, may also provide justification for the selection process. With consistency being fundamental in reducing any potential bias, it would not be appropriate to include the dorsoplantar view joint assessments without the lateral to correspond, as this would contradict the definition of foot osteoarthritis provided by the authors (any joint in either view graded two or more for presence of either osteophytes or joint space narrowing). The grading system used in the LFA atlas differs from that used in the K&L grading as can be seen in table 1, and will be further discussed as a limiting factor in Chapter 4.

Table 1 Comparison between definitions of individual grades

	Kellgren and Lawrence grading	**LFA**	
	Osteophyte & Joint Space Narrowing	**Osteophyte**	**Joint Space Narrowing**
0	None	Absent	None
1	Doubtful	Small	Definite
2	Minimal	Moderate	Severe
3	Moderate	Severe	Joint fusion – at least one point
4	Severe	*Grade 4 not included*	

The LFA has been an important advancement in the interpretation of radiographic osteoarthritis in the foot, however, the atlas has not yet been widely used due to its recent development and publication. Although the atlas is of paramount importance in researching osteoarthritis of the foot, it is important to recognise some of the key limitations that exist, which are documented and explored extensively in Appendix 15. The atlas uses two views for evaluation; the dorsoplantar and lateral, but heterogeneity exists in defining standard procedure of radiographic views (Rankine 2009; Younger et al. 2005). Aside from the basic scoring criteria, the atlas does not provide guidance or narrative information for the evaluative process of joints, which can prove challenging for new users. A further limitation of the atlas is that the population used for the images is unknown in terms of demography (racial variation, gender, age and medical health) and there is the possibility that this may affect the reliability and repeatability in other populations. Furthermore there are limitations in excluded aspects of the atlas and the transferability of the atlas to individual cases. The talonavicular joint osteophytes are not assessed and there is no apparent justification provided, and possible

deformities (eg. Hallux valgus) are not considered within the atlas. These are not the only challenges within the atlas, as identified by Pereira et al. (2011) who explored the impact of definitions on prevalence and incidence and identified high heterogeniety among hip, knee and hand studies.

The LFA limitations could be addressed with the following suggested recommendations;

- Written guidance to the atlas.
- More consistency in pictures whilst also ensuring that any other variables which may affect findings of the aspect being measured are removed.
- Additional information on demographic variation and deformities in the context of foot osteoarthritis.
- Justification for items not being included in the atlas.

A review of the literature would suggest that no definition using clinical criteria has been provided to identify osteoarthritis specific to the foot. A Cochrane review by Zammit et al. (2010) on treatment options for the hallux identified osteoarthritis as presenting with localised pain, stiffness and enlargement of the joint. Goldring and Goldring (2006) include additional symptoms; signs and symptoms of inflammation which include pain and stiffness (previously discussed) and loss of mobility. Having moved away from early conceptual thinking that osteoarthritis is a bone surface defect, Goldring and Goldring (2006) further expound understanding of structural changes in osteoarthritis as progressive loss of articular cartilage; increased subchondral plate thickness; formation of new bone at the joint margins (osteophytes); the development of subchondral bone cysts and the formation of calcified cartilage at the articular hyaline cartilage and adjacent subchondral bone junction.

2.8. Management of foot osteoarthritis and context of wellbeing

The benefit of podiatric healthcare provision is under-investigated. However, preliminary research specific to the improvement of the treatment of inflammatory arthritis in patients using a newly formed service in New Zealand has shown a significant difference in patient reported outcomes (Rome, 2013). Although crude in terms of methods used for identifying the disease, pathological complaint and treatment specific reduction in foot pain, the research highlights the need for and value of this service among the general population suffering with musculoskeletal conditions.

The effect of disability resulting from foot osteoarthritis is less well known in terms of the effect on the general population and healthcare economy (Menz and Morris 2005). However, in broader terms musculoskeletal conditions including osteoarthritis have a significant impact on health and

social care systems and this has been recognised by the World Health Organisation and the United Nations (Woolf and Pfleger 2003). Estimates of one in six people affected by symptomatic foot osteoarthritis suggest that there is a significant societal impact resulting from the disease (Roddy et al. 2015). However, it is evident that foot pain is often overlooked, for instance, strategies adopted in healthcare promotion (as publicly accessible domains online), encourage higher activity levels such as the 'Walking for Health' (http://www.walkingforhealth.org.uk), 'Change4Life' (http://www.nhs.uk/change4life) and 'Couch to 5k' (http://www.nhs.uk/LiveWell/c25k) campaigns which must make the assumption that its target population have the good foot health required to be able to carry out these activities. Yet despite the lack of attention to and value placed on foot health, foot problems and osteoarthritis are predicted to continue to escalate in their societal and economic demand (Chen et al. 2012). As these programmes to aid the prevention of diabetes, obesity, heart conditions and strokes are the focus of good health, they require an appropriate level of foot health in the first instance to be achievable by the general population.

2.9. Foot Pain

Foot pain is described by Hawke and Burns (2009) as 'an unpleasant sensory and emotional experience preceding perceived damage to the area distal to the tibia and fibula' and has been attributed to direct trauma, musculoskeletal overload, infection, or systematic or proximal pathology. Pain is, however, complex and is recognised as being multifactorial (Flores and Hochberg 2003) (see appendix 4). Understanding is further problematised by consideration of the type of pain and of specific aspects of the body such as the foot (Menz and Morris 2005). Following the development and establishment of the Manchester Foot Pain and Disability Index (MFPDI), there has been a rise in research related to foot pain. Although primarily used in relation to 'disabling foot pain', the tool has been used as a basis for defining 'foot pain' through differing criteria. The MFPDI has become generally accepted in the literature as being used for this purpose (Buchman et al. 2010; Laslett et al. 2012; Thomas et al. 2004), and more so than for its primary purpose in defining 'disabling foot pain', despite an apparent lack of agreement on the definition (See figure 6 for heterogeneity of summarised definitions of foot pain).

As foot pain is a common and potentially disabling symptom (Otter et al. 2010), it would be expected that foot pain should be a central concept influencing the treatments provided by clinicians, yet it is an area that has seemingly received little attention. As a crude estimate, Hawke and Burns (2009) suggest that at a given time point, one quarter of the Australian population experience foot pain, whilst Thomas et al. (2004) established a prevalence of 22.9% pain in the United Kingdom. The

overall pooled prevalence of foot pain was documented in a meta-analysis by Thomas et al. (2011) as 24% specific to 'frequent' pain whilst others have reported foot pain prevalence rates ranging from 9.9% to 41.6% using differing definitions of foot pain (Cho et al. 2009; Badlissi et al. 2005). More detailed analysis showing differing definitions among studies can be seen in appendix 4.

Hill et al. (2008) established an overall foot pain prevalence of 17.4%, however, the categorisation of 'foot pain' was amassed with other symptoms such as 'aching' and 'stiffness'. Shortcomings of the study were identified in the use of simplistic data collection methods such as a single question for defining foot pain rather than the validated MFPDI (Menz et al. 2007), and undifferentiated types of pain. Even so, the main published finding that foot pain affects nearly one in five people provides an interesting comparison with the one in six found to have symptomatic osteoarthritis by Roddy et al. 2015). Although this is a thought provoking observation, the heterogeneity of the research methodologies and designs makes this a crude comparison and these findings should be considered with caution. Importantly, the authors emphasised that foot pain epidemiology is a distinctly under-researched area and the need for development of related themes was emphasised.

A recurrent limitation of recall bias emerges through the studies reporting foot pain. Buchman et al. (2010) considered musculoskeletal pain chronicity around the body but required participants to identify if they had experienced pain or aching for no less than one month within the last year. It is also of note that the authors recognised the low prevalence of pain when compared with other studies, perhaps indicative of the underestimated pain by participants' self-reporting, a well-recognised limitation of self-reporting. Clinician based reporting of patient pain (current pain presenting at the time of clinical assessment) is an under investigated area. To the author's knowledge, from extensive review of the literature, the relationship and relevance of clinician diagnosed pain and patient reported pain has not been considered. It is therefore unknown how clinician diagnosed pain compares with patient reporting, or if either has any relationship with the clinical presentation in the foot.

Hill et al. (2008) suggest that establishing effective foot pain research would increase knowledge and understanding of foot pain models. In turn, this would enable better management of foot pain and would establish the appropriateness of current provision of podiatry care for the rising demand in health care. Aside from potentially halting or reversing the lower limb heath related quality of life associated with foot pain, Hill et al. (2008) also identified that foot pain in the general population should be managed more effectively with podiatric service provision.

2.10. Foot Joint Pain (Arthralgia)

A number of papers have been unable to show an association between structural changes (osteophytic or joint space narrowing) in osteoarthritis and pain (Kornaat et al. 2006; Lane et al. 2004). However, associations have been established through investigation of the hands. Kortekaas et al. (2011) established a 'dose-dependent' association between pain and structural changes consistent with osteoarthritis. Associations are made using differing methods for the structural changes (joint space narrowing and osteophytes) when assessing for pain. However, the authors reiterate that associations are independent of osteophytes and joint space narrowing. Buchman et al. (2010) also made an association showing the increased likelihood of hand pain if foot pain is present. Although there are few papers which can support any association between pain and structural change in osteoarthritis, it is still an important consideration. This research on joint extremities provides a further rationale for investigating possible relationships in the foot as this has seldom been the focus of research, and extremity regions have been shown to manifest similar pathological presentation.

From a systematic search strategy, only five articles of relevance were identified with a longitudinal design specific to the foot. Of these, two were prospective studies. The first by Hill et al. (2008) was a nested study and was established from the North West Adelaide Health Study. However, the nested study was only based on one time point and placed equal focus on cross-sectional associations. The study did not use validated measures for assessing foot pain. The second study by Buchman et al. (2010) focussed on musculoskeletal pain and incident disability and again did not use a validated tool. The study simply used two questions, the first being temporal and specific to self-reported joint pain and the second being a temporal question identifying pain in five areas of the body (including the foot). A longitudinal study on knee pain by Soni et al. (2012) highlights the deficit of basic descriptive data in the foot. The authors identified pain patterns such as asymptomatic, persistent, incident or intermittent pain and the consistency (or lack of) pain at each time point. Gay et al. (2014) explored the concept of foot joint pain in the context of body mass index (BMI) with follow-up of patients being five years following baseline. Prevalence of foot joint pain was shown to increase by 5% to 26.6% at follow-up with statistical adjustment showing a positive correlation with increased BMI.

With the recent rise of research on foot osteoarthritis, a consistent trend can be observed where authors have only collected and analysed data relating to the first metatarsophalangeal joint (1st MTPJ). One such paper by Munteanu et al. (2012) using the Foot Health Status Questionnaire

(FHSQ), found a poor association between the radiographic severity of structural change to the 1st MTPJ and the severity of symptoms. Although only inclusive of one joint in the foot, this information provides insight into the relationship between radiographic structure and patient reported symptoms in the foot in terms of severity. This key clinical finding demonstrates a need for further exploration of foot osteoarthritis that seeks to provide an important clinical application, particularly in terms of basing clinical decision-making on a patient's experience of pain. Furthermore, this heightens the awareness around the complexity of pain as a multifactorial concept, but specific to the foot. This limitation of research focusing on one joint, namely the 1st MTPJ, has been recognised by Roddy et al. (2013) and research has begun to include a wider range of joints in the foot (Roddy et al. 2015; Menz et al. 2007).

Few studies have explored cross-sectional associations or the relationships between pain and structural manifestations of osteoarthritis. Laslett et al. (2012) investigated radiographic osteoarthritis and musculoskeletal pain, however, pain in the study was generalised, in that it was collected alongside pain in other parts of the body. This creates the possibility that memory recall bias could result in unrecognised pain and consequent under-reporting of foot osteoarthritis. The findings revealed an association with quality of life and foot pain (along with other areas of the body) and supported previous findings that pain rather than radiographic osteoarthritis was a better predictor of disability. Buchman et al. (2010) in a similar study design, discovered that musculoskeletal pain in one site increases the risk of pain in other areas, for instance, pain in the feet increased the odds by almost eleven fold of having pain in the hands. However, only generalised associations were established between risk factors for pain and sites of pain rather than specifically identifying associations, such as in the foot. Most notably, the authors identified the uncertainty in association between musculoskeletal pain and disability and discussed the multifactorial element of this association.

Despite the lack of evidence of foot pain and its association with foot joint pathology, Roddy et al. (2015) investigated foot joint pain in the context of osteoarthritis. The investigators considered joints from five areas of the foot, first metatarsophalangeal joint (1st MTPJ), first and second cuneo-metatarsal joint (CMJ), navicular first cuneiform joint (N1stCNJ) and the talonavicular joint (TNJ)) based on the LFA. This work was the first, to the authors' knowledge, to explore symptomatic foot osteoarthritis across the foot using the LFA. The research had a clear and focussed aim with a robust methodology and large older population on which to carry out a cross-sectional analysis. However, longitudinal associations were not explored. The study also excluded participants who had no

presence of pain, ‘asymptomatic foot osteoarthritis’. Consequently they were limited to analysing structural changes of symptomatic foot osteoarthritis and were unable to compare these changes between symptomatic and asymptomatic presentation in patients. Finally, the recognition of pain was based on patient self-reported outcomes without the inclusion of any clinical assessment and therefore subject to the usual issues of recall bias. Although pain is anecdotally insensitive when tested by a clinician, this is very poorly documented in the literature. It is therefore a worthy area of consideration when characterising pain in pain focused research. With minor interest expressed in the CASF study (Roddy et al. 2011) and the use of dynamic testing documented (Edwards et al. 2012), this is an area in need of more attention for the benefit of focused clinical and research based knowledge, regardless of outcome.

Pain is a complex area, from its definition, to the individual’s susceptibility to pain, to the process of identification. Focusing on an area comprising of multiple joints and structures adds to the complexity of knowledge and understanding.

Literature surrounding the definition of foot pain raises some important questions; ‘what characteristics should be considered as important in constituting the experience of foot pain?’ should this be inclusive of ‘pain’ as an isolated item or should this encompass ‘pain’, ‘aching’ and ‘stiffness’ as denoted by Hill et al. (2008). Further to this concept, several authors include pain in regions of the foot such as the plantar fascia and nails. This brings to light a whole new meaning of pain whereby all contributory aspects of pain have been recorded by the authors. This concept could be considered as a ‘global foot pain’ approach as opposed to a ‘foot joint pain’ approach as highlighted by Garrow et al. (2000), Thomas et al. (2011) and Gay et al. (2014). Global pain is a concept briefly discussed by Leveille et al. (2008) whereby the authors collected data for both global foot pain and the specific location of pain, both captured effectively in the opinion of the authors by using the Foot Assessment Clinical Tool.

By considering global foot pain, it is inclusive of pain which is both superficial and deep but also pain which can be conclusively or more effectively attributed to a particular pathology through observation or clinical assessment. Within foot osteoarthritis specific investigations, aspects of pain are excluded such as nail pain and plantarfasciitis, perhaps to place a more focused investigation on pain attributable to osteoarthritis. However, this raises another issue, in that foot pain may be recorded and not appropriately adjusted for subsequent information when superficial pain is

identified. Yet again, it should be questioned whether or not this process of elimination devalues the importance of a person's superficial pain.

Review of the literature reveals three key themes among studies relating to types of data collection for reporting foot pain. The first being '**Generalised Foot Pain**' **(Generalised FP)** (reported by all 'foot pain' articles but often reported without further differentiation when reported alongside pain from other areas of the body). The second considers '**Foot Joint Pain**' **(FJP)** which tends to be reported as 'joint symptoms' and is often presented as an undifferentiated overview of the foot. The final apparent theme, '**Global Foot Pain**' **(Global FP)** refers to pain in specific locations of the foot encompassing many aspects such as superficial skin and nail pathologies. Examples of foot pain data collected from the literature are shown in table 2.

Table 2: Pain assessments within the literature

Article	Type of assessment of pain
(Hill et al. 2008)	Generalised Foot Pain, Global FP
(Garrow et al. 2004)	Generalised Foot Pain, Global FP, FJP (non-specific)
(Dufour et al. 2009)	Generalised Foot Pain, Global FP
(Thomas et al. 2004)	Generalised Foot Pain, Generalised FP
(Badlissi et al. 2005)	Generalised Foot Pain, Global FP (limited), FJP
(Menz et al. 2006)	Generalised Foot Pain, Generalised FP
(Gay et al. 2014)	Foot Joint Pain FJP

2.11. Co-existence of radiographic foot osteoarthritis and foot pain

The most important development in the understanding and knowledge of osteoarthritis was the publication of work by Roddy et al. (2015). In this work, the authors described prevalence of radiographic foot osteoarthritis among a symptomatic population to be 16.7% overall among participants (with a range of 3.9%-7.8% among the five joints of the LFA). It is of note that this was specific to a symptomatic population and the prevalence within a general population not defined by the presence of pain is unknown. Munteanu et al. (2012) described the factors associated with foot pain (identified using the FHSQ) and osteoarthritis in the first metatarsophalangeal joint (using the LFA). However, the prevalence of co-existing foot pain and first metatarsophalangeal joint prevalence was not described and excluded severe radiographic osteoarthritis. Similarly, Menz et al. (2015) investigated descriptive characteristics with the presence of radiographic foot osteoarthritis, where foot pain as a characteristic could be calculated in the dorsal 1st MTPJ and plantar 1st MTPJ as

19.8% (n=66; N=333) and 9.9% (n=33; N=333) respectively. Further to this, Bergin et al. (2012) concluded in a small study of participants that pain among participants with radiographic 1st MTPJ osteoarthritis was high. It is of note that data were presented according to the individual scores of the LFA and was not presented in the described format. Prevalence of co-existing radiographic foot osteoarthritis in a symptomatic population was found to be low in this UK based study population.

2.12. Pathophysiology of bone marrow oedema and its relevance to arthralgia

As previously described (section 2.11.), challenges exist in describing any strong association between structural changes in osteoarthritis and pain in the foot since at the joint level, pain is difficult to assess. This has been attributed to the lack of innervation in cartilage (Hunter et al. 2008). It has also been shown that radiographic features identified for evaluation in osteoarthritis have weak associations with pain (Zhang and Jordan 2008; Arden and Nevitt 2006).

Bone marrow oedema (recently considered though not exclusively known as bone marrow lesions) is recognised using magnetic resonance imaging or ultrasound to identify hypersignal contrast from water sensitive sequences in the bone marrow known as T2-weighted images (Eriksen 2015; Flores and Hochberg 2003; Wildi et al. 2010). However, it is noteworthy that bone marrow oedema is not an exclusive characteristic of osteoarthritis and exists in other rheumatological conditions. Patel (2014) explains that pain within the lower limbs including the feet, is likely to be due to bone marrow oedema when synovitis is not present. Patel (2014) also describes the involvement of bone marrow oedema as a less common occurrence in the foot and ankle when compared to the hip and knee.

Bone marrow lesions are often recognised through focal loading which can most often be identified in valgus aligned knees with histopathological findings demonstrating microfractures (or trabecular alterations) (Wildi et al. 2010). Other features include subchondral sclerosis, subchondral bleeding of the bone marrow, bone marrow fibromyxomatous transformation, cellular infiltration of hypervascularity and finally bone marrow oedema (Taljanovic et al. 2008; Li et al. 2008). Importantly, however, bone marrow has been identified as a less common characteristic and, as a separate diagnostic entity, loses sensitivity to the changes that are occurring in osteoarthritis (Taljanovic et al. 2008; Hunter et al. 2008). Although some authors such as Wildi et al. (2010) describe difficulty with describing an association between bone marrow oedema or lesions and pain, others including Taljanovic et al. (2008), Driban et al. (2013) and Radojcic et al. (2017) have conclusively identified corresponding increasing pain with increased bone marrow oedema (or for the latter two authors, bone marrow lesions) in advanced cases of hip osteoarthritis. This demonstrates the importance of

bone marrow oedema or lesions, particularly when considering the joint as an organ with its many tissue components. For the foot and ankle, this has been demonstrated in a recently developed scoring system with the inclusion of the dichotomous variable for bone marrow oedema when investigating osteoarthritis (Halstead et al. 2017). However, whilst of critical importance to the development of research in foot osteoarthritis, the currently limited validity in other populations and the low sample size (N=15) dictate the focus of diagnostic work in osteoarthritis toward the currently more established methods of radiographic diagnosis. Furthermore, the cost of magnetic resonance imaging is high compared to radiography, which would be problematic for larger sample studies (Duryea et al. 2010). However, the development of magnetic resonance imaging in radiographic foot osteoarthritis will enable osteoarthritis to be more appropriately considered in respect of being a 'whole organ' involvement of the joint (Braun and Gold 2012). This will help bring foot-specific research into line with the investigation of more novel concepts that have been considered in joints which have had more attention in research such as the hip and knee.

2.13. Natural history of radiographic osteoarthritis and foot pain

It is evident that research relating to the natural history of radiographic foot osteoarthritis is limited. This is in respect of the progression and incidence using longitudinal data in radiographic foot osteoarthritis. The prevalence of radiographic foot osteoarthritis has been explored to an extent in recent years, as previously described. However, progression of research to consider the natural history remains an unexplored area. Furthermore, there is no known research considering the natural history of foot pain as a co-existing characteristic with radiographic foot osteoarthritis.

However, research on the natural history of radiographic hip and knee osteoarthritis is more developed in understanding and knowledge. Arden and Nevitt (2006) recognise the slow development of radiographic osteoarthritis of the knee, and stable progression with improvement over long periods is recognised as existing infrequently. This is supported by the findings of Leyland et al. (2012) who demonstrated a low incidence and progression of radiographic knee osteoarthritis over a 15 year period at approximate five year intervals. Arden and Nevitt (2006) identified the variable course of radiographic hip osteoarthritis whereby symptoms and structural change rarely correlate in the majority of patients in terms of improvement in both characteristics. The conclusion of this is that knee, hip and hand osteoarthritis are clearly understood in terms of natural history, with no mention of current advances in foot osteoarthritis. Whilst recommendations for future research arising from meta-analysis in radiographic knee osteoarthritis recommend exploring the mechanisms underlying osteoarthritis, research in foot osteoarthritis is yet to provide detailed descriptions of these (Srikanth et al. 2005).

Whilst investigating hand osteoarthritis, cumulative incidence was identified to be higher among the women studied in the Framingham study (Chaisson et al. 1997). Oliveria et al. (1995) identified overall incidence at 1% with increased incidence with increased age, higher rates among women, and a 'levelling off' at the age of 80 among Fallon community residents in Boston. By comparison, Felson et al. (1995) found 2% to have incident knee osteoarthritis in the Boston Framingham study and expounded this through the investigation of symptoms which identified painful knee incidence among 1%. The more recent work by Leyland et al. (2012) found cumulative incidence in the knee to exist at 2.3% among women of the London based Chingford study on women only, where the incidence would have been expected to be higher due to the exclusion of men. Although not specific to the foot, this provides an understanding of research relevant to the natural history in an anatomical extremity with multiple joints and within the lower limb. The need to explore literature on other joints highlights the need for better and more detailed understanding of the natural history of radiographic foot osteoarthritis and foot pain. The use of early research in the natural history of radiographic osteoarthritis of joints is befitting to the conclusion of Arden and Nevitt (2006) that descriptive epidemiological characteristics are well understood for the hand, hip and knee. However, this also highlights the limited research and need for investigation within the foot of these descriptive epidemiological characteristics and how considerably neglected and overdue research in this area is.

2.14. Literature review findings

2.14.1. Summary of the evidence gap

It is evident from review of the literature that effective identification of osteoarthritic change is through observation of the presence of osteophytic lesions and joint space narrowing using an imaging modality such as radiographic imaging. It is also clear that in order to investigate osteoarthritis in the foot, it is most appropriately measured using the LFA which has become generally accepted among research groups through its increased use in studies. Not only is there limited research on foot osteoarthritis but few research groups have considered foot osteoarthritis in the context of pain. Furthermore, no studies have considered co-existing foot radiographic osteoarthritis and foot pain using a general population as the study participants (as opposed to participants being defined by the presence of foot pain symptoms). It is of paramount importance to understand the disease affected population and natural history of foot osteoarthritis in the general population. This is not just for diagnostic purposes but to establish a better foundation for research leading to more appropriate and individualised treatments.

For the purposes of the MPhil, the feasibility of the investigator carrying out the evaluations of the radiographic images used must be established in order to be able to consider descriptive work in foot osteoarthritis. It is therefore necessary and of foremost importance for the investigator to carry out the (intra-rater) reliability work as the first study in the MPhil project. Establishing the reliability will ensure any descriptive data produced in the thesis, including work on prevalence, incidence, associations or risk factors are repeatable, accurate, valid and appropriate results. Finally, in establishing robust methods, it is essential to consider proof of concept to explore the existence of radiographic foot osteoarthritis and any associations with foot pain in order to be able to analyse these in greater detail using larger participant samples. Chapter 3 will explain the methodology to enable the aims and objectives outlined in this chapter to be fulfilled.

2.14.2. Research Questions;

(1) Can the study investigator (PMc) use the LFA to reliably describe the presence of osteoarthritis in the feet using repeated measurements of existing foot radiographs from the 'Chingford 1000 women' study?
(2) What is the prevalence of radiographic foot osteoarthritis, foot pain and the co-existence of both characteristics?
(3) What is the natural history of radiographic osteoarthritis, foot pain and the co-existence of both characteristics?

2.14.3. Aims and objectives of study 1, 2 and 3 investigations (Chapters 4, 5 & 6)

2.14.3.1. Study 1 (Chapter 4)

Aim: To establish the feasibility and user reliability of a single researcher (PMc) using the LFA to determine radiographic foot osteoarthritis within a UK based general population of women.

Objectives were:

- To describe intra-rater reliability of an observer (PMc) in scoring radiographic foot osteoarthritis using the LFA.
- To establish the LFA atlas as valid in determining the presence of radiographic foot osteoarthritis in the Chingford 1000 Women study.
- To establish the most appropriate technique in scoring radiographic foot osteoarthritis using the LFA.

2.14.3.2. Study 2 (Chapter 5)

Aim: Investigate and describe the prevalence and distribution of radiographic osteoarthritis occurring within the foot and co-existing foot pain in a UK population-based cohort of older women.

Objective weres:

- Define the prevalence, severity and distribution of radiographic osteoarthritis in the foot among a UK population-based cohort of older women.
- Characterise the prevalence of foot pain among older women from a UK population-based cohort of older women using different pain parameters.
- Define the prevalence of radiographic foot osteoarthritis with co-existing foot pain among older women.

2.14.3.3. Study 3 (Chapter 6)

Aim: To show the natural history of radiographic foot osteoarthritis, foot pain and the co-existence of both characteristics in a UK population-based cohort of older women over time, from middle age to older age.

Objectives were:

- Investigate the change in prevalence of radiographic foot osteoarthritis over a 17 year time period (year 6 to year '23') in a cohort of older women from a UK population.
- Explore the natural history of radiographic foot osteoarthritis and the first metatarsophalangeal joint with co-existing foot pain over time.

2.15. Summary

This chapter has detailed the published literature currently available using the appropriate search strategy and has explored the areas and concepts lacking consideration in research with little or no literature available. Consequently, focused objectives, aims and research questions have been defined for the thesis. The aims and objectives were identified to facilitate the research questions considering the feasibility of the LFA among the Chingford 1000 Women study, prevalence and natural history of foot osteoarthritis and the co-existence of foot pain whilst using a robust methodology.

Chapter 3: Chingford 1000 women study

3.0. Introductory chapter summary

This chapter considered the study design required to fulfil the aims and objectives of the studies, application of these to the Chingford 1000 Women study, and the recruitment process and participant samples established at baseline and follow-up. The content of this chapter was in respect to answering the primary MPhil research question;

'What is the prevalence and natural history of radiographic structural change in foot osteoarthritis and co-existing foot pain in a UK population-based cohort of women?'

3.1. Study design

The MPhil thesis used quantitative methods and was epidemiological, using cross-sectional and longitudinal designs throughout to observe phenomena. This contributed to answering the over-arching question on foot osteoarthritis and foot pain in the general population. The main outcomes included; Foot osteoarthritis, Foot pain and the co-existence of radiographic foot osteoarthritis and foot pain.

Two datasets (Chingford 1000 Women study of baseline at year 6 and follow-up at year '23') were used for this thesis. Year 6 x-ray dataset was instrumental to the intra-rater reliability of the investigator using the LFA, whilst year '23' explored the best technique whilst using the atlas due to the additional lateral projections being available within follow-up x-ray.

The year '23' x-ray and pain dataset enabled descriptive work on foot osteoarthritis with foot pain and the respective key pain patterns showing co-existence of both. The baseline and follow-up datasets were used together using the dorsoplantar projection only for the purpose of consistency (as year 6 did not include the lateral projection). This provided descriptive work to investigate the natural history with longitudinal observations using year 6 participant data matched with year '23' participant data.

Descriptive and analytical methods were used and were incorporated into each study using the principles of epidemiology.

3.2. Study participants

Data from participants were taken from a community-based cohort recruited at baseline with no known pathology, through GP practices. The 'Chingford 1000 Women study' is based in North London and was established in 1989 as a prospective longitudinal study investigating osteoporosis

and osteoarthritis. Hart et al. (1999) described the women as being 98% Caucasian with the majority being considered lower to middle class, the 'white collar' workers. In terms of smoking statistics, hysterectomy rates, height and weight, these were all considered to be normative statistical values consistent with UK 'normal' participants. Data collection points are outlined with data on those who attended clinic and x-ray and those lost to follow-up or who had died, in figure 3.

The Chingford 1000 women study, for which data have been collected up to year '23' was used to fulfil the aims of the MPhil project. The defining characteristics which make it a cohort study include the area (North East London) from which participants were recruited and the female gender. Livshits et al. (2009) reported that age was also a defining characteristic. Participants from the Chingford based study ranged between 45 and 64 years of age at baseline in 1989. The study was selected on the principle of being able to carry out both cross-sectional and longitudinal research on the participants. It is well recognised that prospective studies are often expensive, time consuming and require a considerable amount of administration (Bowling 2009). For this reason, the pre-existing Chingford based study was used to fulfil the aims of the project. It is acknowledged that the use of the Chingford study introduced several limitations with respect to the study design.

3.3. Study sample size of return study participants

The sample size for the Chingford 1000 women study (N=1003) was predetermined at the conception of the study in 1989 and decided upon with the primary purpose of being set up as a prospective study. The other determinants of the sample size included the non-returning participants for reasons of; passing away, being physically unable to attend or being a full time carer (amongst other reasons). The response rate for year 6 was N=846, 84.3% on baseline attendance. The response rate for year '23' was N=332, 33.1% which was calculated from the baseline attendance (figure 3).

3.4. Data selection and participant recruitment

Year 6: It is understood that the same approach was taken for year 6 as with year '23', with contact with participants made by the research manager to discuss the upcoming visit and establish if participants would like further information regarding this. The year 6 visit consisted of a clinical visit with clinical and self-reported variables collected. Additionally x-ray imaging was carried out and included the dorsoplantar projection of both feet recorded using traditional plain films.

The year 6 data were used for studies 1 and 3 which involved use of the x-rays. At the time of data collection, all participants involved in the year 6 visits gave informed consent and ethical approval had been granted prior to the commencement of any research. An application was made to a local

ethics committee which approved the use of extracted data from the year 6 visit and the follow-up clinical and radiographic foot assessments of participants at year '23'. Ethical approval for year 6 data was granted by the Waltham Forest and Redbridge local Research Ethics Committee (reference: LREC R&WF 96) and sponsorship was provided by Whipps Cross Hospital Research and Development unit.

Year '23': contact was made (by the research assistant) to patients with a telephone conversation explaining the study follow-up visit for year '23' and participants were asked if they would like further information. Patients were sent study information and further contact was made to establish if they were interested in being involved with the follow-up visit and where responses were positive the participants were booked into a clinic appointment. Once at the clinic, participants had all aspects of the year '23' study explained to them and if happy to proceed, gave their written consent for each part of the study (Appendix 5). For the clinical foot assessments, a summary of what the foot assessments entailed was discussed and the MPhil student ensured there was implied or verbal consent before carrying out the assessments. Analysed clinical characteristics and the procedures carried out in the year '23' follow-up are summarised in appendices 6 and 16 respectively.

The year '23' data were used in study 1, 2 and 3 of the thesis. An application was made to the project data ethics committee and approval was granted by NRES Committee South Central – Oxford A, which was received in May 2013 (REC number: 84131) (See appendix 7). Participants involved in year '23' gave informed consent (appendix 5) prior to the commencement of any research taking place. Participants were contacted and were only advised to come if they were physically fit enough to attend. The management of the Chingford 1000 Women study is detailed in the governance section (3.5).

Foot x-rays were taken at year 6 and '23' study visits with year '23' x-rays being taken from April 2014 to July 2015. Both years enabled the combined prevalence of foot osteoarthritis and foot pain at different time intervals. This provided the data required to explain the natural history of osteoarthritis and foot pain within a UK population-based cohort of older women.

3.5. Governance

3.5.1. Ethical committee approval

Year 6: Ethical approval was given by the Waltham Forest and Redbridge local Research Ethics Committee (reference: LREC R&WF 96) and sponsorship was provided by Whipps Cross Hospital Research and Development unit.

Year '23': An application was made regarding the use of the Chingford 1000 Women Study on an NHS site to the project data ethics committee. Approval was granted by NRES Committee South Central – Oxford A which was received in May 2013 (REC number: 84131) (See appendix 7).

3.5.2. Data handling and storage

Professor Nigel Arden was the principal investigator of the Chingford 1000 Women study at the time of the year '23' follow-up and a team at the Botnar research centre at the University of Oxford were overseeing all affairs related to the study. Additional approval was acquired with a formal application for access and use of data from year 6 of the Chingford 1000 Women study (see appendix 7). This was acquired via the Chingford Study Scientific and Ethical Access Committee and also included a 'Data Transfer Agreement' between the University of Oxford and University of Southampton.

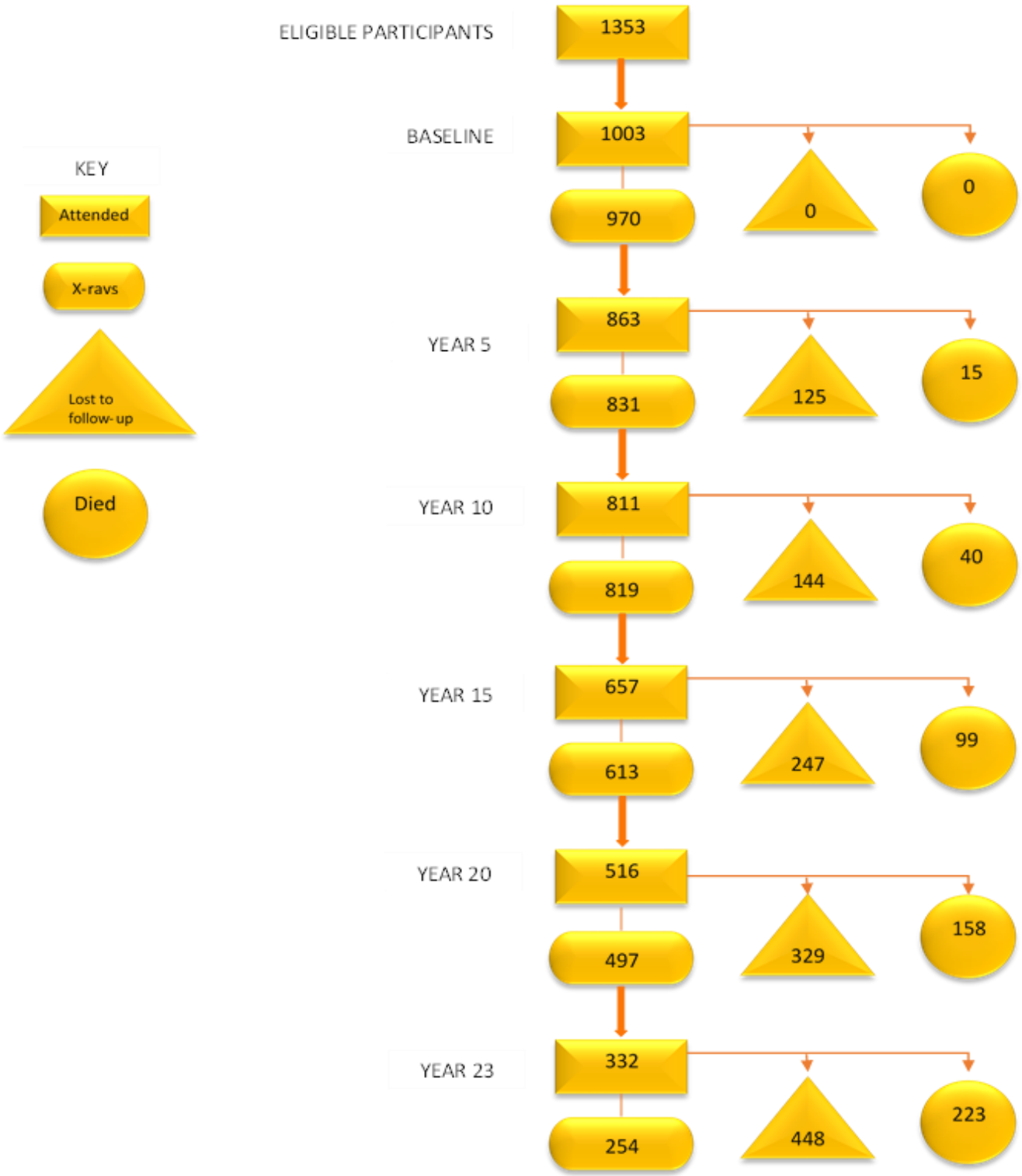
3.5.3. Patient risks and avoidance measures

The participants of the study at year '23' were within an older age category, therefore considerations were made in terms of what would be expected of the participants and possible further assistance required as a result.

For the clinical assessments, participants were required to lie on a hospital couch whilst foot assessments were carried out. Participants were required to stay in relaxed standing position for no longer than 15 minutes to provide enough time for all of the foot assessments. Participants unable to stand for longer than such periods were excluded from the assessment.

Finally, due to the radiographic assessments of the feet, there was exposure to radiation beyond what is considered normal for standard care of patients for those who chose to be involved in the second phase of the study (radiographic foot assessments). However, the level of radiation was very low and the risk was considered to be trivial.

Figure 3 Flow diagram of successive data collection points in the Chingford 1000 women study



**Adapted from MPhil thesis work by Leyland (2012)*

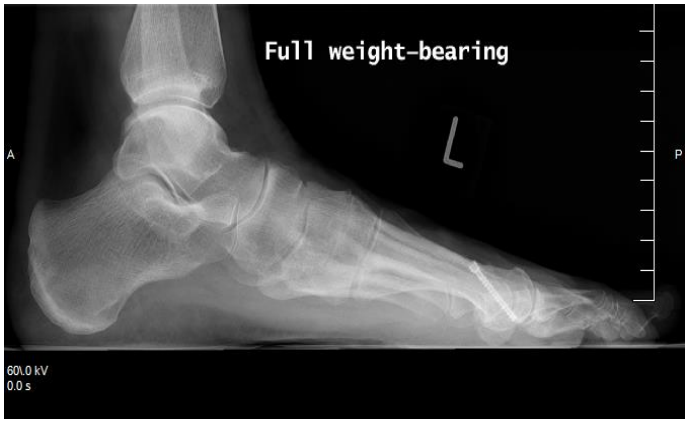
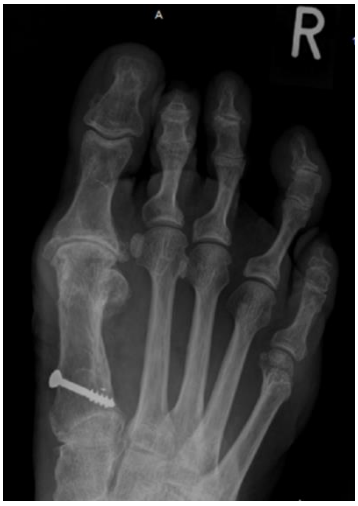
[correct at completion of data collection for year '23']

3.6. Radiographic scoring of participant images

Radiographic foot osteoarthritis is defined by the LFA scoring method (Menz et al. (2007) as *"present if a score of 2 or above is documented for either osteophytes or joint space narrowing, from either the dorsoplantar or lateral projection."*

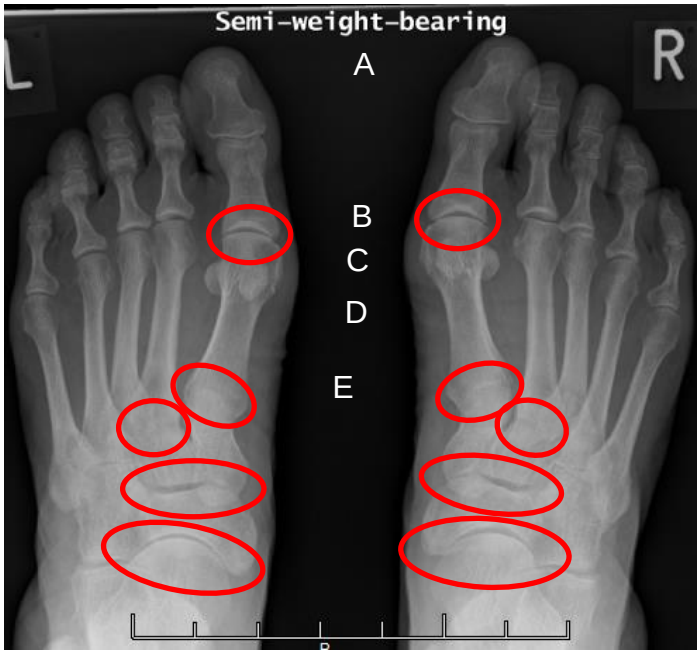
Menz et al. (2007) agreed this definition to reflect the typically used case definition of the two and above Kellgren and Lawrence grading, and the authors similarly placed equal weighting on the two radiographic views and on observations of osteophytes and joint space narrowing. The joints assessed in the atlas include the 1st metatarsophalangeal joint (1st MTPJ), 1st cuneo-metatarsal joint (1st CMJ), Navicular 1st cuneiform joint (N1stCJ) and Talonacular joint (TNJ) (Figures 4 and 5). The authors suggest that using two views more easily identifies radiographic structural change. Of note, the Chingford 1000 Women study cohort year 6 foot radiographs were collected twelve years prior to the development of the foot atlas and, more importantly, prior to digital radiographic technology. X-rays were therefore recorded using plain film radiographs at year 6 with only dorsoplantar projections of both feet included within the study design. In keeping with x-ray advancements, the year '23' foot radiographs exist as digitised foot x-rays with dorsoplantar and lateral views. Table 3 demonstrates the practical outworking of dorsoplantar and lateral projection.

Table 3 Images of dorsoplantar and lateral projections used

Lateral view	Dorsoplantar view
	
	

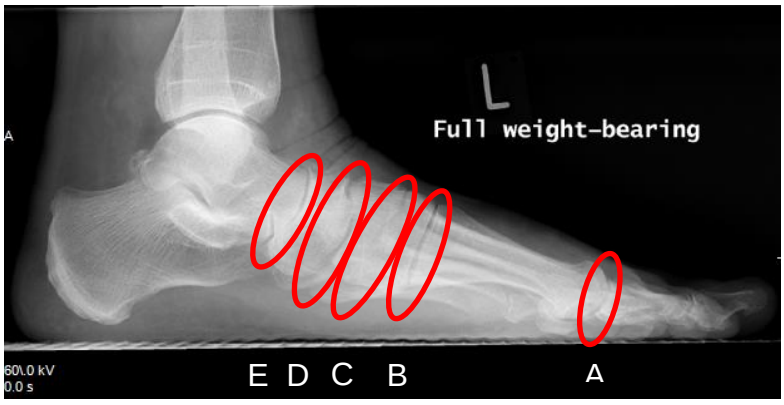
**Radiographic images are from Chingford 1000 women study and clinical images are author's own*

Figure 4 Radiographic foot image showing dorsoplantar projection joints in LFA (taken from year '23' x-rays)



	Joint	OP grade	JSN grade
A	1st MTPJ	0-3	0-3
B	1st CMJ	0-3	0-3
C	2nd CMJ	0-3	0-3
D	N1st CJ	0-3	0-3
E	TNJ	*N/A*	0-3

Figure 5 Radiographic foot image showing lateral projection joints evaluated in LFA (taken from year '23' radiographs).



	Joint	OP grade	JSN grade
A	1st MTPJ	0-3	0-3
B	1st CMJ	0-3	0-3
C	2nd CMJ	0-3	0-3
D	N1st CJ	0-3	0-3
E	TNJ	0-3	0-3

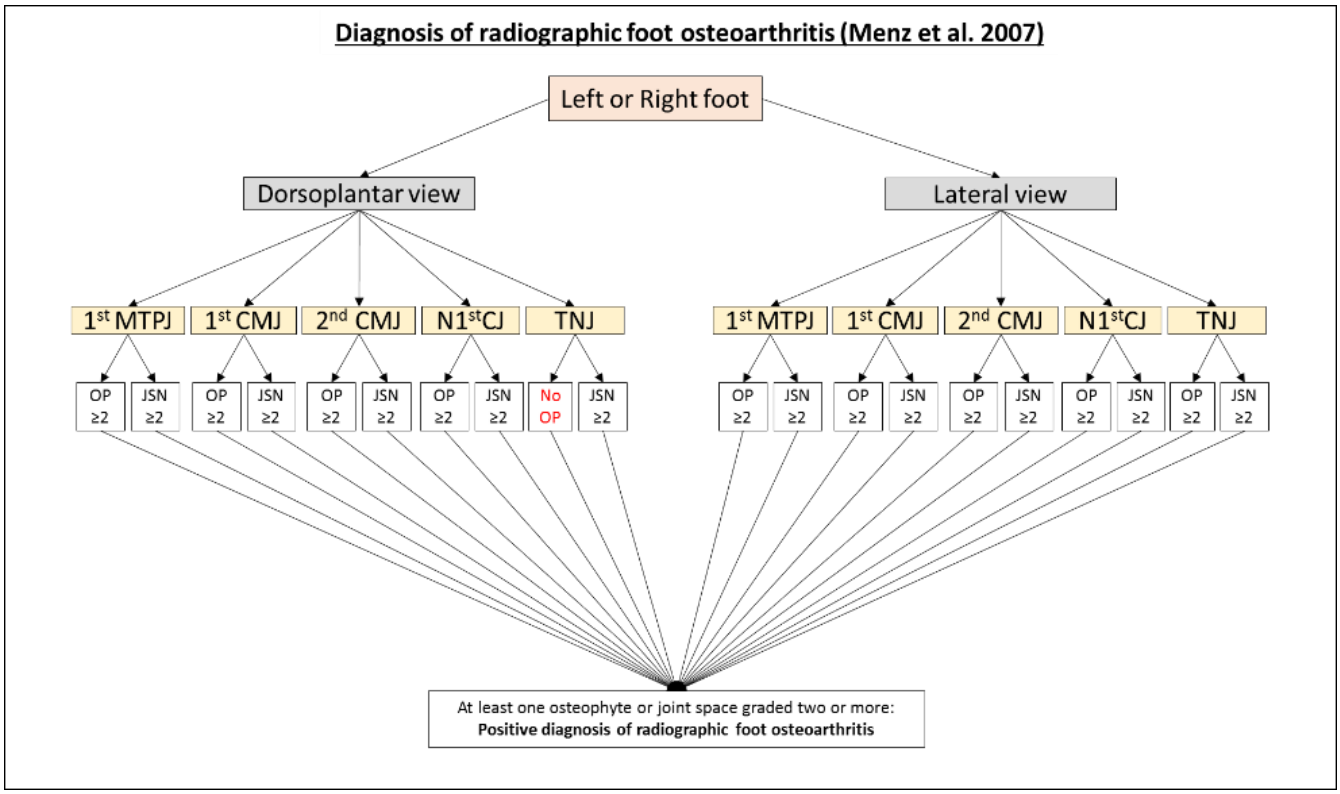
In order to describe prevalence of radiographic osteoarthritis, raw scorings of data (handwritten on printed dataset sheets) were entered by hand into SPSS statistical program for all joints in both projections (year 6 dorsoplantar only), of both feet for both osteophytic and joint space narrowing characteristics. This amassed to 38 scorings and at this level enabled the presentation of specific scorings of radiographic foot osteoarthritis through running descriptive statistics functions to acquire

prevalence for each joint. To establish diagnoses in joints, scores of ‘0’ or ‘1’ were converted to ‘0’ to represent absence of radiographic osteoarthritis and scores of ‘2’ or ‘3’ were converted to ‘1’ to represent presence of radiographic osteoarthritis. Running the descriptive statistics function enabled the presentation of the prevalence of osteoarthritis in each joint. To consider diagnosis of osteoarthritis in the foot or feet (polyarticular evaluated radiographic osteoarthritis), the sum of joint entries was calculated for each participant (only ‘0’ and ‘1’ at this level of analysis). Where no osteoarthritis was diagnosed in any of the joints, the sum was ‘0’ and scores of ‘1’ to ‘19’ or ‘38’ indicated a diagnosis of osteoarthritis in the foot or feet respectively.

Foot pain was calculated with the same approach of coding as osteoarthritis. Absence of pain was coded as ‘0’, presence of pain as ‘1’ and combining locations to acquire the sum of pain established the prevalence of pain in regions of the foot and the feet through use of the descriptive statistics function.

To consider co-existence of (polyarticular evaluated) radiographic osteoarthritis and foot pain, foot pain presence was coded in double digits ‘10’ (‘0’ for absence) and osteoarthritis presence in single digits ‘1’ (‘0’ for absence) which provided the following coding; ‘00’ for participants with no pain or diagnosis of osteoarthritis, ‘10’ for non-osteoarthritis painful feet, ‘1’ for non-painful radiographic osteoarthritis and ‘11’ for painful osteoarthritis. Finally, foot osteoarthritis and foot pain were stratified according to age and BMI through use of the cross-tabulations function in SPSS.

Figure 6 Diagnosis of multifaceted radiographic foot osteoarthritis in multiple projections



3.7. Training undertaken by the Podiatrist for carrying out radiographic scoring

All radiographic scoring was carried out by the same researcher (PMc) who is a UK HCPC registered Podiatrist and who undertook training in 'Good Clinical Practice'. Appropriate training was also undertaken in accordance with the (IRMER) guidelines supplied by the Board of the Faculty of Clinical Radiologists:

'After suitable training there may be no statutory impediment to a non-medically trained person reporting a radiological examination and making technical observations, but a person without medical training cannot reasonably be expected to provide a medical interpretation.'

The researcher (PMc) followed the scoring framework principles outlined by the LFA.
The standard operating procedures for year '23' radiographic foot imaging developed by the MPhil student can be seen in Chapter 4.

Mentorship in scoring technique was also gained from the supervisory team who include a professor of podiatry (CB) and two professors of rheumatology (NA, MD). A consensus session took place with a radiographer based in the University of Keele (MM) to ensure that the techniques used by the researcher (PMc) were standardised with an experienced user of the LFA.

Through the collaborative work that was carried out between the MPhil student and other professionals, it was established that different grading techniques were employed whilst using the LFA. It was found that these differing techniques present among atlas users was due to the opportunity for interpretation without a supporting narrative or guidance incorporated into the atlas. The extent of the narrative or guidance provided with radiographic imaging was non-existent beyond the definition of specific joint osteoarthritis and foot osteoarthritis according to the variables of radiographic projection and feature of osteoarthritis. It was found that atlas users used either a conservative or a sensitive approach when providing a score for an x-ray feature of osteoarthritis that was ambiguous. It was therefore suspected that the former of these could result in underestimating presence (and therefore prevalence) of osteoarthritis whilst the latter overestimated presence (and prevalence).

In addition to this potential interpretation-type bias, a discussion emerged and was led by the MPhil student regarding the ability to score all features of all joints in all studied participants using the LFA. This inevitably leads to the exclusion of joints that could not be graded with absolute certainty or the inclusion of joints whereby all joints are allocated a score according to the atlas. This approach may also be subject to a bias of overestimating or underestimating severity of osteoarthritis features and the presence of osteoarthritis. It was therefore important to investigate these two concepts of underestimating or overestimating severity and presence of osteoarthritis and the influence of including or excluding joints that cannot be scored with absolute certainty. This led to the development of the three techniques described in Chapter 4.

Although the investigation of these concepts and possible biases was not part of the intended project, the MPhil student identified this as an important investigation to ensure best methods were used. This was a change that the supervisory team agreed with, and ensured that reliable results were produced whilst also being able to provide a recommendation for the way atlas is interpreted.

3.8. Inclusion and exclusion criteria

Study 1, 2 and 3 differed in their aims and objectives which are explained in chapters 4, 5 and 6. These aims and objectives are reflected in the inclusion and exclusion criteria seen in table 4. Baseline data are included also as a reference point for studies 1, 2 and 3.

Table 4 Inclusion and Exclusion criteria

Study	Baseline		Study 1		Study 2		Study 3	
	Part of recruitment process	**Justification**	**Intra rater reliability**	**Justification**	**Prevalence of foot rOA & pain**	**Justification**	**Natural history of foot rOA & foot pain**	**Justification**
Inclusion criteria	Women	Population characteristics of interest	*Same criteria as baseline.*		*Same criteria as baseline.*		*Same criteria as baseline.*	
	Live in Chingford		Participants who attended x-ray; year 6 and '23'.	Foot x-rays are the primary outcome (study 1).	Participants who attended year '23' x-ray.	Reporting was of older women.	Participants who attended year 6 and '23' x-rays.	Foot x-rays are the study 3 primary out-come requiring base-line & follow-up with paired participants to consider prevalence & natural history.
	Aged 40 and above				Participants who attended year '23' clinical visit	Data on pain were required to consider osteoarthritis co-existence of pain	Participants who completed foot pain data.	Foot pain is a primary outcome of study 3 & requires baseline & follow-up paired par-ticipants to consider natural history.
Exclusion criteria	Participants not part of the C1000W study	The C1000W cohort has chosen for use with this study.	*Same criteria as baseline*		*Same criteria as baseline.*		*Same criteria as baseline.*	
	Too physically unwell to attend.	Duty of care to the participants involved in the research.			year 6 x-rays.	year '23' lateral view x-rays are in-keeping with the LFA. Prevalence of year 6 is presented in Study 3 with a smaller paired sample.	Participants who did not attend year 6 or '23' x-rays.	See inclusion criteria.
	Men	The established C1000W study was appropriate & financially viable study for the thesis studies.					Participants who did not complete data at year 6 or '23'.	See inclusion criteria.

Appendix 6 shows the recruitment process which took place specific to year '23', which was in accordance with the ethics approved standardised operating procedures of the study. The flow chart also shows the order and process in which data collection procedures were carried out. Research staff included the MPhil student (a qualified Podiatrist), a phlebotomist and the research assistants who oversaw much of the managerial and administrative work related to the study, including the upholding of good clinical practice.

3.9. Chingford 1000 Women study data collection environment and timescale

The timeframe of data collection for the MPhil project was dependent on the logistics of the Chingford 1000 Women study follow-up visit at year '23'. With limited clinical spaces and older aged participants, space had to be negotiated and convenient times had to be arranged with the participants. Two sessions for clinical rooms were available one day per week. This meant that the study data collection took place between November 2013 and July 2015. Radiographic imaging was carried out within a mobile NHS unit and a private hospital as no radiographic imaging facilities were available on site. Challenges existed with setting up radiographic imaging which required institution approved contracts to enable these collaborations. This meant that this part of the data collection process was operational between April 2014 and July 2015.

3.10. Summary

Having identified the aims, objectives and research questions of the thesis, this chapter outlined definitions for radiographic foot osteoarthritis and foot pain for use within the Chingford 1000 Women study. It was established that the Chingford 1000 women study, despite the recognised limitations, was an effective means of fulfilling the aims and objectives set out by this project. Having recruited participants and focused on osteoarthritis with previous years of relevant data, this study can be considered a suitable resource for fulfilling the aims and objective of the project. Studies 1 (chapter 4), 2 (chapter 5) and 3 (chapter 6) provide the practical outworking of the methodologies discussed in this chapter with presentation of results, discussions, identification of strengths and limitations and final conclusions.

Chapter 4:
Study 1 – Feasibility in scoring radiographic foot osteoarthritis using the LFA

4.0. Introductory chapter summary

This chapter outlines the feasibility of scoring using a radiographic atlas in terms of reliability, validity and appropriateness. Aims and objectives of the study are detailed and methods are explained. The study includes various scoring techniques. Results are presented and discussion and conclusions are drawn, whilst also identifying strengths and weaknesses of the study.

4.1. Introduction

There is a low level of reporting on radiographic foot osteoarthritis (OA) and where research exists, it is often limited to the first metatarsophalangeal joint (MTPJ) (Trivedi et al. 2010). The main body of research on radiographic foot OA comes from Australia, primarily with a cohort from the North-West Adelaide Health Study which has examined a community-derived population (Menz et al 2007; Menz et al. 2009; Menz et al. 2010)). Data also exist for UK populations, but this relates solely to symptomatic populations presenting in primary care (Roddy et al. 2015).

Methods of reporting and defining radiographic foot osteoarthritis are often poorly described in the literature. However, the Kellgren and Lawrence (1958) atlas and the LFA by Menz et al. (2007) are the most frequently documented (Trivedi et al. 2010; Iagnocco et al. 2013). This lack of methodological standardisation across studies, and in particular the evident heterogeneity in case definitions, is an important contributor to the lack of evidence regarding foot osteoarthritis (Trivedi et al. 2010). The best validated method for measurement of radiographic osteoarthritis is the Australian developed foot atlas (LFA) (Menz et al. 2009; Roddy et al. 2015). Inter-rater reliability for this has been published previously by Menz et al (2009) and the use of this atlas will be explored in this study using a UK population-based cohort of older women.

Therefore, the aim of this study was to establish the feasibility and reliability of a single researcher (PMc) using the LFA to determine radiographic foot osteoarthritis using existing radiographs in the UK based Chingford 1000 women study cohort. In order to demonstrate feasibility, the following areas are explored;

- Reliability
- Appropriateness
- Validity

The LFA is described relative to the standard techniques and a revised technique to identify the extent of disease impact according to changes consistent with osteoarthritis in the feet. The atlas is also reviewed according to its appropriateness for use in scoring radiographic foot osteoarthritis in an established longitudinal dataset.

The relevance, background and challenges of reliability of using the LFA are discussed and different approaches of statistical analyses will be considered and evaluated in terms of their potential impact on the results of the latter chapters (5 and 6). However, the primary focus relates to the repeatability of results by an individual (test retest reliability of the study investigator).

RESEARCH QUESTION

Can the study investigator (PMc) use the LFA to reliably describe the presence of osteoarthritis in the feet using repeated measurements of existing foot radiographs from the 'Chingford 1000 women' study?

4.2. Study aims and objectives

Aim: To establish the feasibility and user reliability of a single researcher (PMc) using the LFA to determine radiographic foot osteoarthritis within a UK based general population of women.

Objectives:

- To describe intra-rater reliability of an observer (PMc) in scoring radiographic foot osteoarthritis using the LFA.
- To establish the LFA as valid in determining the presence of radiographic foot osteoarthritis within the Chingford 1000 Women study.
- To establish the most appropriate technique in scoring radiographic foot osteoarthritis using the LFA.

4.3. Methods

4.3.1. Study Design

The design is quantitative and incorporates the observation of a cross-sectional sample with the purpose of establishing measurement reliability of the study investigator (PMc). Specifically, phenomena are measured using scientific methods and analysed to compare differences which can be interpreted by reasoning and logical deduction. Using these methods, it is recognised by Bowling (2009) that reliability, validity and appropriateness are key challenges. The methodological underpinning and justification for this approach is explored in section 4.3., Chapter 4.

To identify 'appropriateness' of the atlas, taking account of the technique for scoring radiographic foot osteoarthritis to subsequently determine prevalence (Chapter 5) and natural history (Chapter 6), a descriptive comparison is presented with stratification of presence of osteoarthritis according to each foot, joint and radiographic projection.

4.3.2. Study 1 (Chapter 4) Justification of methods: Feasibility in scoring radiographic foot osteoarthritis using the LFA

In order to describe prevalence and natural history of radiographic foot osteoarthritis and the co-existence of both characteristics, data produced must be reliable in terms of the user of the LFA applied to the Chingford 1000 Women study. The feasibility of these things is crucially important for the subsequent data produced in study 2 and 3. Feasibility encompasses concepts in validity, reproducibility, accuracy and appropriateness relevant to the use of the LFA in the Chingford based study. These concepts are defined in table 5.

Table 5 Feasibility explored

Area of feasibility testing	**Definition**	**How areas of feasibility have informed the study**
Validity	Internal validity: An instrument or tool is deemed valid when it has been tested repeatedly on populations it was created and assigned to (Bowling 2009). External validity: This is where research findings are deemed generalizable to wider populations being studied (Bowling 2009).	Validity (specifically internal) has been considered in the previous work of Menz et al. (2009), as noted by Roddy et al. (2013). The most notable effect on internal validity for the thesis is the availability of only one radiographic projection at baseline (year 6) in the Chingford 1000 women study. As a result, internal validity should be tested. External validity was considered through the work of Roddy et al. 2015 who produced results comparable with Menz et al. (2007).
Reproducibility	Reproducibility is the variation that occurs in measurements of a subject made in changing conditions. Changing conditions can include; measurement methods instruments, different observer's measurements or measurements made over a period of time (Barlett & Frost 2008).	In this instance, the observer for the thesis studies (PMc) was not directly linked to any of the LFA authors and therefore it was evident that the observer in this case would need to be tested. To consider observer reproducibility, measurements were considered using percentage agreement and kappa scores to ensure radiographic evaluation of foot osteoarthritis was reliable.
Accuracy	Accuracy is the deviation of the observed value that occurs from the true value (Windolf et al. 2008).	The 'gold standard' for evaluating radiographic foot osteoarthritis is through the use of MRI of the foot. However, further validation of the use of this MRI in osteoarthritis of the foot needs to be considered, particularly in direct comparison to x-ray. Therefore the most appropriate method was to consider inter-rater reliability against expert opinion to build a body of evidence for use of the LFA. Menz et al. (2007) established moderate agreement between observers and stated that the atlas was a useful measure of the condition of single examiners or consensus gradings

		being used. This negates the need for inter-rater reliability work in this thesis as it has previously been established with optimal conditions identified.
Appropriateness	Appropriateness is when extraneous factors (to the purpose and nature of the instrument or tool) do not affect the outcome measure (Capuzzi & Gross et al. 2013).	Through consensus meetings and training, it became evident that a challenge of appropriateness was in the standardisation of evaluation technique as many aspects of scoring radiographic images were open to interpretation. The literature also makes it clear that standardisation in defining radiographic osteoarthritis is unclear. The appropriateness of interpretation technique (the three techniques are described in section 4.3.7.) when using the LFA needed to be considered as this had not been previously explored as there were challenges recognised in standardisation of technique for those external to the original team that developed the atlas.

Reliability is considered by Friis and Sellers (2013 p418) to be the 'same measurement results being reproduced on repeated occasions'. Test-retest describes the strength of a measure, specifically the reproducibility of responses on a scale (Bowling 2009). Reliability is a key factor in establishing the quality of research and when substantiated, represents the ability of the results of a study to be replicated (Stewart 2010). In this instance of establishing reliability using the LFA, intra-rater reliability of the observer (PMc) is also tested.

There are several ways in which reliability can be statistically analysed. These may include Bland Altman plot, intra-class correlation co-efficient, percent agreement and Kappa scores. These areas are explored below with a summary of the methods chosen to analyse reliability of the user of the LFA.

A Bland Altman plot is used in two circumstances: for a comparison of two methods of measurement or for a comparison of a new and established method where, in both cases, the true values are unknown (Myles and Cui 2007). Bland Altman graphs are effective at showing the extent of systematic difference, how values are scattered and any relation between values and measurement

error (for example random error arising from outliers) (van Stralen et al. 2008). It has, however, been discussed that Bland Altman plots do present a difficulty in establishing 'good' or 'bad' agreement and standard deviation is therefore underestimated in narrow limits of agreement, most recognisably in repeated measures (van Stralen et al. 2008).

Intra-class correlation co-efficient (ICC) is a means of identifying the proportion of variability and the systematic difference for a new method (van Stralen et al. 2008). The proportion of variability is that which results from 'normal' variability existing in individuals and is compared with the systematic difference, the variation due to measurement error (Euser et al. 2008). Intra-class correlation coefficient is a measurement relative to reliability and would therefore make it inappropriate as the choice for a statistical test. Key to the reliability work is establishing the variation due to measurement error as opposed to understanding the difference with normal variability. Systematic difference alone is also not sufficient for establishing the reliability of intra-observer results.

Percent agreement is useful in establishing agreement of results. However, it does not consider the agreement beyond chance, where chance is a variable. As percent agreements do not correct for chance, this can equate to misleading results and interpretations (McGinn et al. 2004). Cohen's Kappa overcomes this limitation and provides a proportional agreement on the basis of this adjusted result. Cohen's Kappa coefficient is primarily used to consider nominal data where a value of '0' is representative of the agreement being no better than chance and a value of '1' being representative of a perfect agreement (Bowling 2009).

The categorisation of Kappa scores numerically with corresponding definitions was considered by McGinn et al. (2004) in a teaching article produced by the Canadian Medical Association. The study related to radiological interventions with Kappa being used in the reliability tested diagnostic measures. Due to the relevance of the study to the thesis studies, this was therefore selected as the system of defining agreement of intra-rater reliability with the LFA which can be viewed in table 6.

Table 6 Kappa scores and corresponding definitions

Kappa score	Definitions of agreement (McGinn et al. 2004)
0	**No agreement** beyond chance
0-0.2	**Slight** agreement beyond chance
0.2-0.4	**Fair** agreement beyond chance
0.4-0.6	**Moderate** agreement beyond chance
0.6-0.8	**Substantial** agreement beyond chance
0.8-1.0	**Almost** perfect agreement beyond chance

Key to the results produced in study 2 (Chapter 5) and study 3 (Chapter 6) was establishing the reliability of the observer (PMc) in evaluating radiographic foot osteoarthritis using the LFA. This was established through the repeated scoring of a sample of radiographic images selected randomly. This work was therefore an exploration of the study investigator's reproducibility using an x-ray scoring system which played a vital role in the subsequent studies presented with the thesis.

However, when the atlas was initially used by the investigator for the study (PMc), it was discovered that no technique of evaluation using the atlas or interpretation of results was provided. Through internal and external training and consensus meetings, different methods of assessment were identified whereby some observers using the atlas would score every joint with varying degrees of certainty whilst other recognised the inability to score some joints. It was also noted that where ambiguity of two grades existed ('0' and '1', '1' and '2', or '2' and '3') some researchers scored the presence of osteoarthritis in joints conservatively whilst other took a more sensitive approach. As a result of this, techniques of scoring were devised to incorporate these varying methods that have the potential to impact on the appropriateness of the atlas when evaluating radiographic osteoarthritis in the foot.

Finally, as the Chingford 1000 Women study differed in design with only one radiographic projection available in year 6 data compared to the gold standard described by Menz et al. (2009) whereby two radiographic projections were available, the validity of the LFA needed to be considered. This was investigated within the same Chingford 1000 Women study cohort where only one projection was available, but using year '23' where the availability of both projections existed and could be compared for validity.

To consider reliability and appropriateness, three different interpretations of the LFA were investigated. This was particularly important considering there is no set of guidelines or standards supplied with the atlas to facilitate the generation of reproducible and accurate measurements (the scoring of radiographic osteoarthritis in foot joints). Further to this, Menz et al. (2007) identified through reliability testing establishing high percentage agreements but low kappa scores, that there was likely to be an inherent variability in the interpretation by a given observer when using the atlas. The evaluation of interpretations of the atlas were therefore indicated. As a result, reproducibility and accuracy needed to be explored where there was ambiguity in joint scorings to a lower score (underestimation) and a higher score (overestimation). Additionally, reproducibility and accuracy needed to be explored where there was disparity between the LFA images and participant images such that scoring could not be accurately determined. As a result, three interpretations of the atlas were investigated;

- **Technique 1:** Generally accepted conservative method with ambiguous results underscored (LFA suggested scoring and University of Keele scoring method)
- **Technique 2:** Joints documented as missing where they could not be scored with certainty
- **Technique 3:** Individual joint scorings overestimated

4.3.3. Study participants (foot radiographs)

Foot radiographs were sourced from established participant data, collected as part of the Chingford 1000 Women study (See section 3.2, Chapter 3). For this investigation, a random sample of radiographs, taken from year 6 data, were used to test intra-rater reliability of scoring radiographic foot osteoarthritis using the LFA (Appendix 1). A second, different sample of foot radiographs, taken from year '23' data, were then used to compare two techniques identifed in scoring methods using the LFA to assess validity of the techniques and appropriateness of the techniques for use in the prevalence (study 2) and natural history (study 3) investigations for radiographic osteoarthritis.

Figure 7 Intra-rater reliability procedure

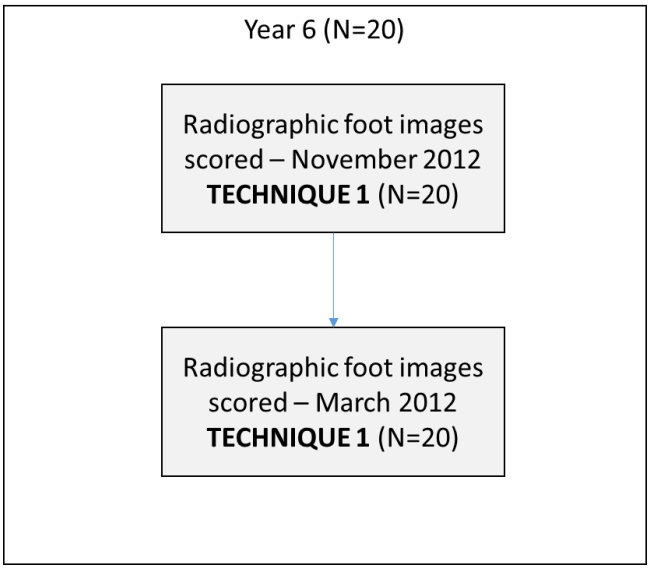
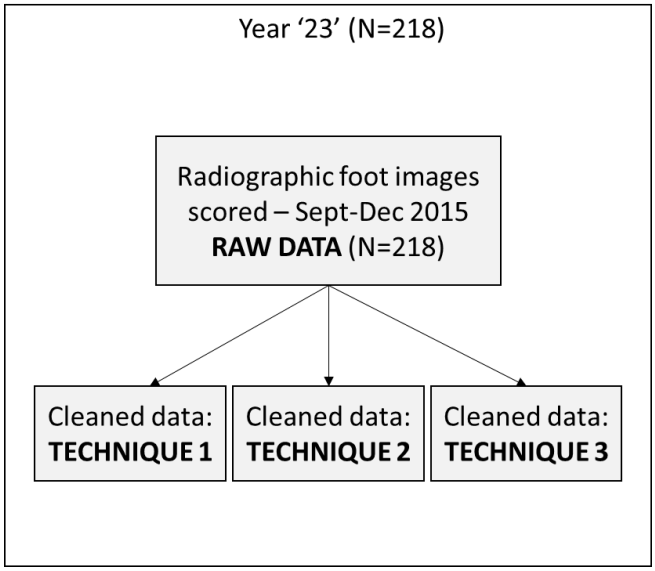


Figure 8 Validity and appropriateness of technique procedure



4.3.4. Data collection for intra-rater reliability of scoring foot radiographs

A convenience sample of foot radiographs from year 6, archived in four age bands, that had been pre-selected by two senior investigators for use in a previous unpublished reliability study (n=93) were used to test intra-rater reliability in scoring radiographic foot osteoarthritis using the LFA scoring method. From the pre-selected sample of year 6 radiographs (n=93), 20 paired radiographs were selected at random using an online software www.randomizer.org (Figures 7 and 8). All radiographs from this sample, (n=20) were scored by the researcher (PMc) in Nov 2012 and then re-

evaluated for a second time more than one year later (March 2014). The time period between the initial radiographic evaluation and the re-evaluation reduced the possibility of observer bias resulting from memory of previous scoring and associated study numbers or the radiographic presentation of OA.

4.3.5. Data collection for scoring foot radiographs to test technique appropriateness

At year '23', 254 participants underwent foot x-rays and 218 of year '23' were used. All foot radiographs were scored simultaneously during the period September to December 2015 according to three techniques:

- **Technique 1** was employed as the accepted technique to be used with the LFA. This involved conservative scoring (underestimated score) and was consistent with the methods used in the CASF and NWAHS.

- **Technique 2** was a revised version of technique 1 that had three components of scoring whereby all joints scored with ungradable joints were included as 'missing'.

- **Technique 3** was a revised version of technique 1 whereby all joints were scored using the LFA, and joints that could not be scored with absolute certainty were scored according to the higher LFA score (i.e. overestimated scores)

4.3.6. Radiographic scoring method for foot osteoarthritis

The LFA approach was identified in the literature review (section 2.7, Chapter 2) as the most appropriate method for determining radiographic foot OA. The LFA scoring method is based on the principles adopted by the Kellgren and Lawrence atlas for grading osteophytes and joint space narrowing. The LFA focuses on 5 of the 32 joints of the foot and uses a four-point scale of 0, 1, 2 and 3 in contrast to the 5 point Kellgren & Lawrence grading (Kellgren & Lawrence 1958). Osteoarthritis is scored on both feet in two radiographic views (dorsoplantar and lateral) (Figures 6). Although the LFA was identified as the most appropriate atlas, the recognised limitations of the atlas are presented in Appendix 13.

4.3.7. Scoring technique using the LFA to determine radiographic foot osteoarthritis

4.3.7.1 Intra-rater reliability: Scoring technique

The authors of the LFA provide pictorial guidance for their scoring system and this technique was employed as the accepted technique to test intra-rater reliability (Technique 1).

Technique 1 was carried out on 20 paired foot radiographs taken from the Chingford 1000 Women study year 6 data, and then repeated 16 months later (N=20) with the investigator (PMc) blinded to the initial scores. Radiographs were identifiable by participant coding. Although it is possible that some detail could have been remembered from the first assessment, the time lapse between the first and second assessments was over one year, which should have ensured that scoring for individuals would have been forgotten.

Consensus work was carried out with Dr Michelle Marshall from the University of Keele, an experienced radiographer with extensive research experience in epidemiology. The radiographer had experience in using the LFA having been given training by the author of the atlas (Hylton Menz) and collaborated in research projects between their respective institutions. This ensured the scoring methods used by the researcher (PMc) were appropriate and comparable to previous research.

4.3.7.2 Validity and appropriateness: Scoring technique

Through receiving training and through consensus meetings for scoring whilst using the LFA, it was established that 'Technique 1' used an interpretative-type approach that may leave the scoring open to potential bias towards over-estimating the prevalence of OA. The possibility that observer interpretation may affect the validity of the final score when the radiographic appearance did not appear to directly correspond with the atlas images was discussed as a potential limitation. As an example, scoring could have been based on other radiographic characteristics known to be consistent with osteoarthritis (such as subchondral cysts) or on assumption of an anatomical feature being present or not present when it is not possible to make an objective decision (such as the identification of joint without visibly seeing the attached bone or its anatomical position).

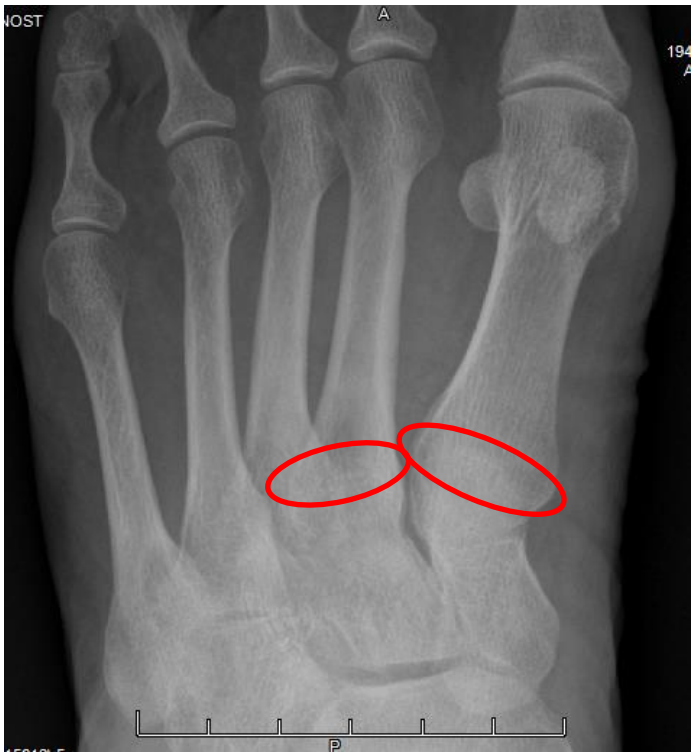
A consensus meeting was held between the researcher and the supervisory team in which revised scoring methods (techniques 2 and 3) were devised by the MPhil student (PMc). Technique 2 involved a detailed approach where each joint assessment was given a grade in the absolute certainty that the structures in question could be identified with features when compared with the

LFA pictorial definitions. All joints considered to be ungradable due to any uncertainty were identified in the raw data as 'U' and coded in the data as 'missing'. Joints in technique 3 that were identified as ungradable in technique 2 were allocated a score that was conservative (i.e. underestimated score/ underscoring). For the purposes of the analyses and discussion, Technique 1 is compared to Technique 2 (joints considered as missing) and Technique 3 (overscored or sensitive).

All joints that were deemed ungradable were marked as 'U' (ungradable) in the data record sheet (raw data). A conservative radiographic score was then also provided in brackets to represent the score that would be allocated if 'U' was not an option (for example U (3) (Table 7 and Figure 9).

To test the appropriateness of the techniques, joints which were difficult to score from the perspective of the observer (PMc), were documented as ungradable (U) but also given a conservative estimate score (ie a lower grade). These joints were documented with a dash ' - ' on the data collection sheet. For example, where an osteophyte in a participant's joint may have been ambiguous to score between a grading of 2 or 3, the researcher (PMc) used the lower grading of '2'. Joints observed with ambiguity in this manner were also marked with a minus symbol (i.e. '2-') (Table 7). This provided the opportunity to consider three techniques through cleaning of data of one raw dataset. Techniques 2 and 3 were assessed against technique 1 for appropriateness using the year '23' foot radiographs as both views were available and all were in a high definition digitised format.

Figure 9 Foot radiograph highlighting disparity between techniques



*The foot radiographs seen here highlight the 1st and 2nd cuneo-metatarsal joints. The isolated joints have been selected on the basis that technique 1 would include a score for the joints whereas technique 2 considers the effect of the joints being unsuitable for scoring.

Table 7 Scoring disparity between techniques whilst using the LFA

	Raw data		Technique 1		Technique 2		Technique 3	
	OP	**JSN**	**OP**	**JSN**	**OP**	**JSN**	**OP**	**JSN**
1st Cuneo-metatarsal Joint	U0-	U3	0	3	-	-	1	3
2nd Cuneo-metatarsal Joint	U2-	U3	2	3	-	-	3	3

4.3.8. Statistics

The data in this chapter were collected by scoring radiographs for presence of foot osteoarthritis in accordance with the methods outlined in section 4.3. Data were hand written whilst evaluations were recorded and after the completion of data collection all data were input into IBM SPSS Chicago software version 22.0.

Bland-Altman plots are effective at presenting mean difference and limits of agreement and are appropriate when attempting to consider comparability of methods through presenting the

differences between methods. However, a limiting aspect of Bland-Altman plots is that it does not enable a method (or in this case reproducibility) to be established as appropriate or suitable for use through interpretation of its measures. However, Kappa considers agreement and where agreement is a result of chance, unlike Bland Altman plots that consider significant differences and do not have a standard of acceptable levels of agreement (Giavarina 2015). This is where Kappa scores differ in providing better interpretation of reliability through quantitative measures, showing the extent of agreement which can be categorised according to a scale (Viera and Garrett 2005; Watson and Petrie 2010). In the case of the studies presented in the thesis, the 'within-observer agreement' (intra-rater reliability) is deemed appropriate (Watson and Petrie 2010). Of note, Kappa has been used to consider the intra-rater reliability of observers using the LFA (Menz et al. 2007; Roddy et al. 2015). Kappa was chosen as the results were categorical in terms of presence or absence of osteoarthritis. The type of data used in establishing agreement for intra-rater reliability was categorical on the basis of a diagnosis of osteoarthritis (scoring as either OA+ve or OA-ve). This means that use of Bland-Altman plots, which present the average of the two scores (original and repeated measure) would not work, as Bland Altman plots rely on interval or ratio data. Ordinal data generated by individual scorings (0-3) were not tested for repeatability as with previous work by Roddy et al. (2013). Notably, the primary focus of studies 2 and 3 involved the diagnosis of osteoarthritis rather than specific scorings within foot joints. As a result, the type of data was nominal, not ordinal, meaning it was not possible to analyse data using weighted Kappa, as indicated in the work of Mandrekar (2011). For tests of intra-rater reliability, the Kappa statistic was therefore selected as the method of analysis, performed using the SPSS program software.

Errors in the measurement of disease are recognised as a source of bias in epidemiological work, and diagnostic techniques should aim to be valid despite full validation of disease measurement rarely being feasible (Coggon et al. 2003). Section 4.3.2. outlined the importance of evaluating measurement error namely systematic differences of which, radiographic projections and observer interpretation of the LFA were most susceptible to this bias in the thesis work. By descriptively comparing the variation of data with prevalence data, it was possible to consider the measurement error of a large number of variables. The importance of measurement error specific to the variation of repeated observer measurements (intra-rater reliability) was also described in chapter 4 (section 4.3.2.). This was carried out using Kappa scores with diagnostic data of a random sample of participants from the Chingford 1000 Women study to establish the extent of variation diagnosing osteoarthritis in both features of osteoarthritis (osteophytic change and joint space narrowing) for each LFA joint by a single observer. Standard deviation (SD) is considered to be an estimated

measurement of variability of the population from which the sample was sourced (Altman and Bland 2015). The sample mean is used to make an estimation of the mean for the entire population and the extent of this variation from the standard deviation is known as standard error of the estimate of the mean (Altman and Bland 2015). As standard error is a precise measurement from the sample to establish a mean within the whole population, this was presented with the kappa results to consider variation. Standard error was presented for both features of osteoarthritis (osteophytes and joint space narrowing) among LFA identified joints of each foot to provide an extensive overview of measurement error for the kappa scores.

The primary analysis of intra-rater reliability scoring of radiographic foot osteoarthritis was formatted into binary data where a positive diagnosis of foot osteoarthritis was considered '1' and no diagnosis as '0'. A Kappa score was then calculated for each assessed joint to consider agreement for osteophytes, joint space narrowing and combinations of the two in each foot. The secondary analysis focused on the diagnosis of rOA individual joints. As in the primary analysis, the Kappa statistic was utilised with agreement considered as '1', and no agreement considered as '0'. For the tertiary analysis for individual joints and osteophytes and individual joints and joint space narrowing, it was not possible to carry out Kappa analysis due to too many zeros ('0'). The P value to establish significance was set at 0.05 (Bowling 2009). For assessment of validity and appropriateness of the two techniques, these are described by non-parametric statistics as frequency (%) of radiographic foot osteoarthritis at person level and at joint level. Differences in prevalence between the two techniques are reported as frequency and range.

4.4. Results

The analysis focuses on:

1. Intra-rater reliability of using the LFA to determine presence of foot osteoarthritis.
2. Validity and appropriateness of two techniques in using the LFA to determine foot osteoarthritis.

4.4.1. Intra-rater reliability (year 6, technique 1)

4.4.1.1. Intra-rater reliability in determining presence of foot osteoarthritis using the LFA, technique 1.

To determine the reliability of the researcher (PMc) in scoring foot radiographs for presence of osteoarthritis, 20 paired foot radiographs were scored at baseline time point (Nov 2012) and then compared to repeat scores that were performed 16 months later (March 2014).

When scores for all joints were considered together, overall agreement for presence of osteoarthritis within the left foot was not computed by the statistics program for all joints, but left foot joint space narrowing demonstrated substantial agreement. Percentage agreement was therefore also presented and demonstrated a high level of agreement.

Table 8 Agreement of the presence of foot osteoarthritis in either left or right feet

	Osteophytes (OPs)	**Joint space narrowing (JSN)**	**OPs & JSN**
Left foot (n=20)	K= No result* PA= 100%[¥]	K= 0.773 PA= 95.0%	K= No result* PA= 100%
Right foot (n=20)	K= No result* PCA= 100%	K= No result [‡] PA= 85.0%	K= No result* PA= 100%

**SPSS could not calculate statistics for all but one item using Kappa as the binary data were constant between baseline and repeat scoring*

[‡]SPSS could not calculate statistics for the RF JSN as there were not enough numbers to compute (all data were constant between participants at repeat scoring).

[¥]Positive percentage agreement (PA)

4.4.1.2. Intra-rater reliability in determining presence of individual foot joint osteoarthritis using the LFA, technique 1.

At the level of the individual joints, overall joints were within 'moderate' and 'substantial' categorisation for agreement (Table 6) in the left foot, substantial agreement was found to occur in the 1st MTPJ (*k*=0.773) and second cuneo-metatarsal joint (*k*=0.615) for joint space narrowing. Although one joint (the second cuneo-metatarsal) in the left foot demonstrated 'fair' agreement for osteophyte (*k*=0.222), joint space narrowing was 'perfect' (*k*=1.000) within the same joint. Kappa scores are presented below in table 9.

In terms of osteophyte, the second cuneo-metatarsal joint in both the left and right foot produced no result. With regard to joint space narrowing, no result was produced for the talo-navicular joint. This lack of kappa score calculation is most likely due to the fact that there were insufficient numbers to compute a result. For clarity, the osteophyte score for the talonavicular joints was not computed as no evaluation could take place without the atlas guidance (Figure 6).

Table 9 Agreement of diagnosis according to radiographic feature in each joint

	Joints	Osteophytes (OPs)	Joint space narrowing (JSN)
Left foot (n=20)	1st Metatarsophalangeal joint	K=0.468 P=0.035 SE=0.203	K=0.773 P=0.000 SE=0.216
	1st Cuneo-metatarsal joint	K=0.222 P=0.292 SE=0.214	K=1.000 P=0.000 SE=0.000
	2nd Cuneo-metatarsal joint	K=No result P=No result CI=No result	K=0.615 P=0.003 SE=0.146
	Navicular 1st cuneiform joint	K=0.583 P=0.009 SE=0.186	K=0.545 P=0.006 SE=0.181
	Talo-navicular joint		K=No result P=No result SE=No result
Right foot (n=20)	1st Metatarsophalangeal joint	K=0.588 P=0.007 SE=0.180	K=No result P=No result SE= No result
	1st Cuneo-metatarsal joint	K=0.368 P=0.069 SE=0.194	K=0.615 P=0.003 SE=0.238
	2nd Cuneo-metatarsal joint	K=No result P=No result SE= No result	K=0.459 P=0.150 SE=0.305
	Navicular 1st cuneiform joint	K=0.694 P=0.002 SE=0.162	K=0.706 P=0.001 SE=0.150
	Talo-navicular joint		K=No result P=No result SE=No result

**Defined as 2 or more on the LFA*

4.4.2. Appropriateness (year '23'; comparison of techniques 1 and 2)

To determine the appropriateness of using the LFA for presence of foot OA, three techniques were compared. 218 paired foot radiographs were scored using technique 1 and then scored again using technique 2 (ungradable joints considered as missing) and technique 3 (underscoring). The results of the percentage presence of radiographic foot osteoarthritis were determined by the three techniques which were compared and differences were observed.

4.4.2.1. Technique 1 compared to technique 2 (ungradable joints as missing)

All first metatarsophalangeal joints (1st MTPJ), first cuneiform-metatarsal joints (1st CMJ), second cuneiform-metatarsal joints (2nd CMJ), navicular-first cuneiform joins (N^{1st}CJ) and talo-navicular joints (TNJ) in both left and right feet for all included foot radiographs (n=218) were scored for presence of osteoarthritis. The presence of foot osteoarthritis was scored according to each view of dorsoplantar and lateral and according to Technique 1 and Technique 2 (ungradable joints as missing) (Table 10).

In all joints, technique 2 demonstrated the same or lower prevalence than technique 1. Differences between techniques ranged from 0.0% to 36.2% and appeared to be indicative of the number of ungradable joints except when projections or joints were combined. This was due to the conditional nature of many variables (projections and joints) on the basis of a diagnosis rather than all variables being required to establish a diagnosis.

Table 10 Prevalence of radiographic osteoarthritis according to five joints and radiographic view according to technique 1 and technique 2 (ungradables as missing).

Foot (n=218)	Joints	RG view	Technique 1 % (n)	Number of ungradable joints‡	Technique 2 (ungradables as missing) % (n; N)	Differences between Technique 1 and Technique 2
Left	1st MTPJ	Dorsoplantar	**27.1** (59)	0	**27.1** (59; 218)	0.0%
		Lateral	**22.9** (50)	21	**13.7** (27; 197)	-7.2%
		Combined	**35.8** (78)	0	**31.2** (68; 218)	-4.6%
	1st CMJ	Dorsoplantar	**45.0** (98)	5	**43.2** (92; 213)	-1.8%
		Lateral	**10.1** (22)	5	**8.5** (18; 213)	-1.6%
		Combined	**49.1** (107)	0	**45.9** (100; 218)	-3.2%
	2nd CMJ	Dorsoplantar	**49.5** (108)	74	**30.6** (44; 144)	-18.9%
		Lateral	**57.3** (125)	75	**27.3** (39; 143)	-30.0%
		Combined	**74.3** (162)	21	**38.1** (75; 197)	-36.2%
	N1stCJ	Dorsoplantar	**19.3** (42)	3	**18.1** (39; 215)	-1.2%
		Lateral	**11.0** (24)	35	**8.7** (16; 183)	-2.3%
		Combined	**24.3** (53)	1	**21.2** (46; 217)	-3.1%
	TNJ	Dorsoplantar	**7.3** (16)	0	**7.3** (16; 218)	0.0%
		Lateral	**21.1** (46)	1	**19.8** (43; 217)	-1.3%
		Combined	**24.3** (53)	0	**22.9** (50; 218)	-1.4%
Right	1st MTPJ	Dorsoplantar	**33.0** (72)	1	**32.7** (71; 217)	-0.3%
		Lateral	**27.5** (60)	25	**16.1** (31; 193)	-11.4%
		Combined	**42.2** (92)	1	**35.9** (78; 217)	-6.3%
	1st CMJ	Dorsoplantar	**47.2** (103)	3	**46.0** (99; 215)	-1.2%
		Lateral	**9.2** (20)	3	**7.4** (16; 215)	-1.8%
		Combined	**49.5** (108)	0	**46.3** (101; 218)	-3.2%
	2nd CMJ	Dorsoplantar	**47.7** (104)	80	**29.7** (41; 138)	-18.0%
		Lateral	**56.4** (123)	76	**22.5** (32; 142)	-33.9%
		Combined	**70.6** (154)	29	**34.4** (65; 189)	-36.2%
	N1stCJ	Dorsoplantar	**17.9** (39)	3	**16.7** (36; 215)	-1.2%
		Lateral	**8.7** (19)	35	**6.6** (12; 183)	-2.1%
		Combined	**22.5** (49)	2	**20.4** (44; 216)	-2.1%
	TNJ	Dorsoplantar	**7.8** (17)	0	**7.8** (17; 218)	0.0%
		Lateral	**15.1** (33)	1	**14.7** (32; 217)	-0.4%
		Combined	**18.3** (40)	0	**17.9** (39; 218)	-0.4%
Both	**Any joint***	**Dorsoplantar**	**81.2 (177)**	**0†**	**78.4 (171; 218)**	**-2.8%**
		Lateral	**83.5 (182)**	**0**	**57.3 (125; 218)**	**-26.2%**
		Combined	**91.3 (199)**	**0**	**83.5 (182; 218)**	**-6.4%**

**Positive diagnosis of radiographic osteoarthritis (LFA grade ≥2) in any joint (1st MTPJ, 1st CMJ, 2nd CMJ, N1stCJ, TNJ)*

†An ungradable joint is only present if it hasn't been superseded by a gradable joint ie. Dorsoplantar view 'All joints' would require ten joints (five joints in each foot) to be ungradable to qualify as being ungradable.

‡Number of ungradable joints column cannot be used as means of checking data between methods (n) as the aforementioned column is a combination of osteophytic change and joint space narrowing. For example in diagnosing joint OA, Established method OP=+ve, JSN=-ve where ungradable method OP=Ungradable, JSN=-ve. Therefore the established method identifies a diagnosis of OA, where the ungradable method does not capture any ungradable joints but also no positive diagnosis of OA.

4.4.2.2. Technique 1 compared to Technique 3 (over-scoring)

The differences between technique 1 and technique 2 (underscoring) exposes a caution that needs to be considered when interpreting the results of any method that doesn't account for ungradable joints. With the exception of the second cuneo-metatarsal joint in both feet, combined differences between methods for each joint never exceeded 7.2% on the left and 11.4% on the right. The method which accounted for ungradable joints was the lowest of all methods explored in total prevalence (83.5%) and showed a difference of 6.4% between the two methods explored in table 10.

All 1st MTPJs, 1st CMJs, 2nd CMJ, N1stCJs and TNJs in both left and right feet for all included foot radiographs (n=218) were scored for presence of osteoarthritis. The presence of foot osteoarthritis was also scored according to each view of dorso-plantar and lateral and according to technique 1 and technique 3 (overscoring) (Table 11).

The second cuneo-metatarsal joint when considered with the technique 3 (underscoring), lowers the joint prevalence to a result much more comparable to the other tested joints. In technique 1, the second cuneo-metatarsal joint exhibits a high prevalence of osteoarthritis (combined views: left foot 74.3% and right foot 70.6%). When compared to technique 2 (underscoring) (combined views: left 38.1% and right 34.4%), there is an impact on the prevalence of osteoarthritis in each joint (left foot difference 36.2%, right foot difference 36.2%).

Table 11 Prevalence of radiographic osteoarthritis according to five joints and radiographic projection showing differences between technique 1 and technique 3 (overscoring).

Foot (n=218)	Joints	RG view	Technique 1 % (n)	Technique 3 Overscoring % (n)	Difference between scoring
Left	1st MTPJ	Dorsoplantar	**27.1** (59)	**38.1** (83)	11.0%
		Lateral	**22.9** (50)	**23.4** (51)	0.5%
		Combined	**35.8** (78)	**42.7** (93)	6.9%
	1st CMJ	Dorsoplantar	**45.0** (98)	**61.9** (135)	16.9%
		Lateral	**10.1** (22)	**15.6** (34)	5.5%
		Combined	**49.1** (107)	**65.1** (142)	16.0%
	2nd CMJ	Dorsoplantar	**49.5** (108)	**55.5** (121)	6.0%
		Lateral	**57.3** (125)	**64.2** (140)	6.9%
		Combined	**74.3** (162)	**79.4** (173)	5.1%
	N1stCJ	Dorsoplantar	**19.3** (42)	**69.3** (151)	50.0%
		Lateral	**11.0** (24)	**16.1** (35)	5.1%
		Combined	**24.3** (53)	**73.4** (160)	49.1%
	TNJ	Dorsoplantar	**7.3** (16)	**22.9** (50)	15.6%
		Lateral	**21.1** (46)	**30.7** (67)	9.6%
		Combined	**24.3** (53)	**43.6** (95)	19.3%
Right	1st MTPJ	Dorsoplantar	**33.0** (72)	**46.3** (101)	13.3%
		Lateral	**27.5** (60)	**28.9** (63)	1.4%
		Combined	**42.2** (92)	**52.3** (114)	10.1%
	1st CMJ	Dorsoplantar	**47.2** (103)	**63.8** (139)	6.6%
		Lateral	**9.2** (20)	**14.2** (31)	5.0%
		Combined	**49.5** (108)	**66.5** (145)	17.0%
	2nd CMJ	Dorsoplantar	**47.7** (104)	**55.5** (121)	7.8%
		Lateral	**56.4** (123)	**60.1** (131)	3.7%
		Combined	**70.6** (154)	**74.8** (163)	4.2%
	N1stCJ	Dorsoplantar	**17.9** (39)	**72.5** (158)	54.6%
		Lateral	**8.7** (19)	**12.8** (28)	4.1%
		Combined	**22.5** (49)	**74.8** (163)	52.3%
	TNJ	Dorsoplantar	**7.8** (17)	**25.2** (55)	17.4%
		Lateral	**15.1** (33)	**26.1** (57)	11.0%
		Combined	**18.3** (40)	**39.9** (87)	21.6%
Both	Any joint*	**Dorsoplantar**	**81.2 (177)**	**92.7 (202)**	**11.5%**
		Lateral	**83.5 (182)**	**89.9 (196)**	**6.4%**
		Combined	**91.3 (199)**	**97.2 (212)**	**7.3%**

*Positive diagnosis of radiographic osteoarthritis (LFA grade ≥2) in any joint (1st MTPJ, 1st CMJ, 2nd CMJ, N1stCJ, TNJ)

All joints in both views were higher in prevalence in technique 3 (over-scoring) when compared to technique 1. Most notably, in the dorsoplantar view, the N1stCJ shows a substantial difference between techniques 1 and 3 in the left foot (50.0%) and right foot (54.6%). The combined views in the N1stCJ also demonstrate high prevalence when comparing the two techniques in the right foot

(49.1%) and left foot (52.3%). When excluding the N1stCJ dorsoplantar and combined views, the left foot ranges from 0.5% to 19.3% with the right foot ranging from 1.4% to 21.6% among views of each joint. Overall, a 7.3% difference existed in the prevalence comparing the established or combined methods.

4.4.3. Validity of the scoring method between the two radiographic views (dorsoplantar and lateral)

4.4.3.1. Technique 2: Foot osteoarthritis according to dorsoplantar, lateral and combined projections

Of the views, the dorsoplantar showed the greatest variation in prevalence of radiographic osteoarthritis followed closely by the combined views with the lateral view demonstrating the lowest joint range difference in prevalence of OA. The combination of views therefore reduced differences in joint range prevalence of osteoarthritis seen in the dorsoplantar projection.

Dorsoplantar projection: The lowest prevalence (talonavicular joint for both feet) and highest prevalence (first cuneo-metatarsal joint for both feet) demonstrate ranges of 35.9% and 38.2% for the left and right feet respectively.

Lateral projection: The lowest prevalence (left first cuneo-metatarsal joint; right navicular 1st cuneiform joint) and highest prevalence (second cuneo-metatarsal joint for both feet) demonstrate ranges of 18.8% and 15.9% for the left and right feet respectively.

Combined projections: The lowest prevalence (left navicular 1st cuneiform joint; right talonavicular joint) and the highest prevalence (first cuneo-metatarsal joint) demonstrate differences of 34.7% and 28.4%.

The prevalence is somewhat affected by the combination with the lateral radiographic projection by lowering the prevalence variation among joints. When considering the variation among the dorsoplantar views specific to joints, the greatest variation existed in the first cuneo-metatarsal joints within the left foot (dorsoplantar, 43.2%; lateral 8.5%) and right foot (dorsoplantar, 46.0%; lateral 7.4%). In four of the joints (1st MTPJ, 1st CMJ, 2nd CMJ and N1stCJ) in both feet, the dorsoplantar view demonstrated the higher prevalence, whereas the TNJ revealed the dorsoplantar view to demonstrate the lower prevalence. This latter anomalous result can be explained by the absence of evaluation of osteophyte in the dorsoplantar view (Figure 6) whilst using the LFA, resulting in a lower prevalence for this joint in both feet.

The dorsoplantar view provides the most variable prevalence estimate of foot osteoarthritis and is therefore the less reliable radiographic projection when using technique 2. Use of the lateral view is an effective approach to osteoarthritis where technique 2 is used and ungradable joints have been eliminated. Having defined the dorsoplantar view as an important view through the descriptive comparison of evaluation methods, it can be concluded that this method should only be used where both radiographic projections have been used to establish the effective prevalence.

4.4.3.2. Technique 3: Foot osteoarthritis according to dorsoplantar, lateral and combined projections

In technique 1, the range of variation between projections among joints was dorsoplantar (left 42.2%; right 39.9%), lateral (left 47.2; right 47.7) and combined (left 50%; right 52.3%).

Dorsoplantar projection: The lowest prevalence (talonavicular joint for both feet) and highest prevalence (navicular 1st cuneiform joint for both feet) demonstrate similar ranges of 46.4% and 47.3% for the left and right feet respectively.

Lateral projection: The lowest prevalence (left first cuneo-metatarsal joint; right navicular first cuneiform joint) and highest prevalence (second cuneo-metatarsal joint for both feet) demonstrate ranges of 48.6% and 47.3% for the left and right feet respectively.

Combined projections: The lowest prevalence (left 1st MTPJ; right TNJ) and the highest prevalence (2nd CMJ) demonstrate ranges of 36.7% and 34.9% respectively.

Of the projections, both the dorsoplantar and lateral projections showed similar variations of prevalence of radiographic OA. The combined views however, demonstrated a lower joint range difference in prevalence of OA. Using a combination of views therefore reduced differences in range of prevalence of OA. This indicates that the combined projection provides the radiographic view with the least variability in the joint prevalence ranges when using the method of overestimation.

When considering the variation among the dorsoplantar views specific to joints, the greatest variation existed in the navicular first cuneiform joints within the left foot (dorsoplantar, 69.3%; lateral 16.1%) and right foot (dorsoplantar, 72.5%; lateral 12.8%). In four of the joints (1st MTPJ, 1st CMJ, 2nd CMJ and N1stCJ) in both feet the dorsoplantar view showed the higher prevalence. However, for the TNJ the dorsoplantar view had the lower prevalence. This anomalous result can be explained by the absence of evaluation of osteophytes in the dorsoplantar view (figure 8) whilst using the LFA resulting in a lower prevalence for this joint in both feet. The most effective approach

to determine radiographic osteoarthritis using technique 1 is with a combination of the two projections (dorsoplantar and lateral).

Although this could be a limitation of the joint evaluation, with a systematic error resulting in the over-diagnosing of radiographic osteoarthritis, this is beyond what would be expected when comparing the established and overscoring or sensitive methods. When excluding the navicular first cuneiform joint dorsoplantar and combined views, the left foot ranges from 0.5 to 19.3 with the right foot ranging from 1.4% to 21.6% among views of each joint. Overall, a 7.3% difference existed in the prevalence comparing the established or combined methods. This result was a significant discovery in understanding the importance of using a well-defined method of evaluation using the LFA. Additionally, it showed the extent or impact of over-scoring on the prevalence of osteoarthritis in the feet.

In the established methods, the range of variation between projections among joints was dorsoplantar (left 42.2%; right 39.9%), lateral (left 47.2; right 47.7) and combined (left 50%; right 52.3%). Although it is well established that radiographic osteoarthritis should be diagnosed with a multi-planar approach on x-ray, the combination of projections showed the largest range of variation among joints. Where there is only one projection available, the dorsoplantar projection has the lesser range in variation among joints which would make it a more accurate and appropriate means of diagnosing radiographic foot osteoarthritis compared to the lateral projection.

4.4.4. Prevalence of radiographic osteoarthritis

4.4.4.1. Prevalence of radiographic osteoarthritis scores in the dorsoplantar projection

Prevalence of radiographic osteoarthritis according to the dorsoplantar projection, individual joints is presented in table 12. Grade 1 demonstrated high prevalence for the navicular 1st cuneiform joints and talonavicular joints in both feet for joint space narrowing compared to all other joints. With grades 2 and 3 (demonstrating the presence of radiographic osteoarthritis), prevalence did not reach as high values as either 1 or 2 (demonstrating absence of radiographic osteoarthritis).

Prevalence of grade 3 radiographic osteoarthritis was particularly low across all joints with the highest prevalence being the 1st metatarsophalangeal joint in the right 8.7% and left 11.0% feet for osteophytic change.

4.4.4.2. Prevalence of radiographic osteoarthritis scores in the lateral projection

Prevalence of radiographic osteoarthritis according to the lateral projection, individual joints is presented in table 13. Grade 0, (no radiographic OA) was consistently high among all joints representing radiographic osteoarthritis specific to the feature of osteophytic change (ranging between 24.8% in the left and 30.7% in the right foot) with joint space narrowing in both feet demonstrating lower values.

Among the joints graded 2 or 3 showing presence of radiographic OA, the prevalence demonstrated low values in both feet with the exception of the 2nd cuneo-metatarsal joint which demonstrated particularly high prevalence for the joint space narrowing feature in both feet. This was seen in both the lateral and dorsoplantar projections (Graphs 1-4). Additionally, the dorsoplantar view demonstrated particularly high prevalence of the 1st cuneo-metatarsal joint osteophytes.

Ungradable joints demonstrated higher values particularly for joint space narrowing in the 1st metatarsophalangeal joint, second cuneo-metatarsal joint and navicular 1st cuneiform joint in both feet. The osteophyte scores demonstrated relatively lower values with one apparent anomalous result in the second cuneo-metatarsal joint in the left (38.1%) and right (39.9%) feet. The lateral view demonstrated higher prevalences across all joints for ungradable joints in both osteophytic change and joint space narrowing features.

Table 12 Prevalence of osteoarthritis stratified according to grading in the dorsoplantar view (N=218)

Foot	Left										Right									
Joint	1st MTPJ		1st CMJ		2nd CMJ		N1stCJ		TNJ		1st MTPJ		1st CMJ		2nd CMJ		N1stCJ		TNJ	
RG sign	OP	JSN	OP	JSN	OP	JSN	OP	JSN	OP	JSN	OP	JSN	OP	JSN	OP	JSN	OP	JSN	OP	JSN
0	85 (39.0)	60 (27.5)	189 (86.7)	36 (16.5)	200 (91.7)	31 (14.2)	207 (95.0)	19 (8.7)		44 (20.2)	73 (33.5)	57 (26.1)	188 (86.2)	31 (14.2)	211 (96.8)	32 (14.7)	193 (88.5)	15 (6.9)		28 (12.8)
1	78 (35.8)	130 (59.6)	26 (11.9)	85 (39.0)	15 (6.9)	79 (36.2)	9 (4.1)	159 (72.9)		158 (72.5)	76 (34.9)	131 (60.1)	29 (13.3)	84 (38.5)	5 (2.3)	83 (38.1)	23 (10.6)	165 (75.7)		173 (79.4)
2	36 (16.5)	12 (5.5)	3 (1.4)	87 (39.1)	3 (1.4)	104 (47.7)	1 (0.5)	36 (16.5)		15 (6.9)	45 (20.6)	17 (7.8)	0 (0.0)	89 (40.8)	2 (0.9)	99 (45.4)	1 (0.5)	35 (16.1)		16 (7.3)
3	19 (8.7)	16 (7.3)	0 (0.0)	10 (4.6)	0 (0.0)	4 (1.4)	1 (0.5)	4 (1.4)		1 (0.5)	24 (11.0)	13 (6.0)	1 (0.5)	14 (6.4)	0 (0.0)	4 (1.8)	1 (0.5)	3 (1.4)		1 (0.5)
Ungradable	2 (0.9)	1 (0.5)	28 (12.8)	10 (4.6)	104 (47.7)	104 (47.7)	14 (6.4)	9 (4.1)		0 (0.0)	2 (0.9)	1 (0.5)	26 (11.9)	6 (2.8)	106 (48.6)	99 (45.4)	14 (6.4)	8 (3.7)		0 (0.0)

Table 13 Prevalence of osteoarthritis stratified according to grading in the lateral view (N=218)

Foot	Left										Right									
Joint	1st MTPJ		1st CMJ		2nd CMJ		N1stCJ		TNJ		1st MTPJ		1st CMJ		2nd CMJ		N1stCJ		TNJ	
RG sign	OP	JSN	OP	JSN	OP	JSN	OP	JSN	OP	JSN	OP	JSN	OP	JSN	OP	JSN	OP	JSN	OP	JSN
0	154 (70.6)	78 (35.8)	200 (91.7)	61 (28.0)	179 (82.1)	7 (3.2)	169 (77.5)	79 (36.2)	146 (67.0)	48 (22.0)	137 (62.8)	87 (39.9)	195 (89.4)	71 (32.6)	177 (81.2)	13 (6.0)	170 (78.0)	101 (46.3)	128 (58.7)	68 (31.2)
1	44 (20.2)	99 (45.4)	13 (6.0)	137 (62.8)	20 (9.2)	89 (40.8)	32 (14.7)	128 (58.7)	48 (22.0)	142 (65.1)	49 (22.5)	88 (40.4)	14 (6.4)	129 (59.2)	22 (10.1)	84 (38.5)	35 (16.1)	104 (47.7)	71 (32.6)	129 (59.2)
2	15 (6.9)	25 (11.5)	4 (1.8)	18 (8.3)	14 (6.4)	109 (50.0)	15 (6.9)	9 (4.1)	22 (10.1)	26 (11.9)	24 (11.0)	31 (14.2)	7 (3.2)	17 (7.8)	10 (4.6)	106 (48.6)	11 (5.0)	11 (5.0)	16 (7.3)	19 (8.7)
3	5 (2.3)	16 (7.3)	1 (0.5)	2 (0.9)	5 (2.3)	13 (6.0)	2 (0.9)	2 (0.9)	2 (0.9)	2 (0.9)	8 (3.7)	12 (5.5)	2 (0.9)	1 (0.5)	9 (4.1)	15 (6.9)	2 (0.9)	2 (0.9)	3 (1.4)	2 (0.9)
Ungradable	26 (11.9)	144 (66.1)	16 (7.3)	14 (6.4)	83 (38.1)	157 (72.0)	41 (18.8)	93 (42.7)	8 (3.7)	3 (1.4)	32 (14.7)	140 (64.2)	13 (6.0)	12 (5.5)	87 (39.9)	163 (74.8)	46 (21.1)	97 (44.5)	5 (2.3)	2 (0.9)

4.5. Summary of findings

4.5.1. Intra-rater reliability

Intra-rater reliability of diagnoses of radiographic osteoarthritis according to features was found to demonstrate a high level of agreement when analysed using percentage agreement. Kappa scores were not effective at determining reliability of diagnoses of osteoarthritis according to features as the data collected were too similar to be computed. When Kappa scores were analysed according to the diagnosis of individual joints according to radiographic feature, adequate reliability was demonstrated with a range of fair to perfect reliability results.

4.5.2. Appropriateness

When considering appropriateness of methods, technique 1 (traditional methods) demonstrated the least variability and provided a conservative estimate of prevalence of each joint in each projection. Technique 2, which involved the recognition of joints that were not comparable to the LFA with absolute certainty and were removed, provided the most conservative prevalence, with technique 3 where joints were overscored providing the highest prevalence. Ungradable joints had a high variability among joints and projections and the overscored joints demonstrated relatively and disproportionately high prevalence.

4.5.3. Validity

The dorsoplantar and lateral projections were considered with respect to validity and it was established that the combination of both projections established the least variability among joints, which is the gold standard identified by Menz et al. (2009). However, it was also noted that if one projection had to be selected, the projection with the least variability was the dorsoplantar view.

4.6. Discussion

In order to ensure robust results in identifying radiographic foot osteoarthritis for the investigation of prevalence (Study 2) and incidence (Study 3), it was essential to assess the feasibility of using the LFA with established existing radiographic data from the Chingford 1000 women study. Three key areas that explored the feasibility were identified to assess the feasibility; reliability, validity and appropriateness.

4.6.1. Intra-rater reliability

The LFA was developed by Menz et al. (2007) to provide a classification atlas for radiographic foot osteoarthritis in order to help standardise the assessment of foot osteoarthritis in epidemiological and clinical research. However, the authors made clear that its usefulness was in the context of single observers or consensus observation whilst using the atlas. Key to the investigations of this thesis is establishing the reliability of the researcher (PMc) when using an atlas to score presence of osteoarthritis in the foot.

This was the first study to investigate the intra-rater reliability of the LFA in a UK cohort of older women. The researcher (PMc) was found to have a high level of agreement between baseline and repeat scoring. Kappa scores did not provide a helpful understanding of the overall agreement according to features in each foot due to the consistency of positive diagnoses of radiographic osteoarthritis. It was therefore necessary to show the positive percentage agreement to provide better interpretation of these results. It is also recognised that percentage agreement is an appropriate measurement of agreement when only two datasets with two values (that is binary data) exist in the analysis (McHugh 2012). Percentage agreement was found to be very high among diagnoses considering the osteophytic change and for both osteophytic and joint space narrowing features, showing perfect agreement. Joint space narrowing demonstrated lower agreement but produced a Kappa score in the left foot of 0.773, considered to be substantial agreement beyond chance according to the classification provided by McGinn et al. (2004). It is accepted that percentage agreement does not capture data which may be chance agreement (Birkimer and Brown 1979) and so these results should be treated with caution. However, individual scores are investigated on a joint level using Kappa scores in table 9 providing a more in-depth analysis of intra-rater agreement.

High levels of intra-rater agreement were demonstrated for scoring of both osteophytes and joint space narrowing in both feet. At the individual joint level, the best levels of agreement were shown to be in the 1st MTPJs and the 2nd CMJs. The 1st MTPJ is the largest of the MTPJs and is not obscured

by other joints when observed in radiographs. These findings are consistent with those of other investigators. Menz et al. (2007) described overall percentage agreement for inter-rater reliability as ranging from 72% to 97% between joints where weighted Kappa was 0.13 to 0.87 demonstrating 'slight to excellent reliability'. The authors also considered the reliability of the overall foot osteoarthritis score. Standard error was also presented and demonstrated small measurement error supporting the construct that there was appropriate reliability of the results.

Importantly, an issue with the study design has been recognised when using Kappa, which may have resulted in lower Kappa scores. However, this is not explained in terms of whether osteophyte and joint space narrowing are considered in combination or as separate entities, within a joint, foot or both feet. Mandrekar (2011) identified that where there is a particularly high prevalence within diagnostic studies, this may result in lower Kappa scores and so caution has to be taken when interpreting the results in these instances. This is where percentage agreement helped to interpret the Kappa scores with crude agreement between baseline and repeated observations contributing to the better understanding of intra-rater reliability in this study. Further to this, research by Menz et al. (2007) and Roddy et al. (2013) carrying out very similar work appeared to be subject to the high agreement low Kappa paradox whereby chance corrected ratio affected the observed agreement (Feinstein and Cicchetti et al. 1990). It is likely the same issue occurred within study 1. However, percentage agreement of 85-100% was not dissimilar to the 86-99% established by Menz et al. (2007). Without any detailed description and interpretation, it is difficult to draw many useful conclusions from this exercise. The main conclusion that can be deduced from this work is that inter-rater reliability was established to have an overall lesser but acceptable degree when compared to the intra-rater reliability testing of the MPhil student evaluating Chingford foot x-rays. Relevant also, is the fact that the author responsible for developing the LFA was also the tested observer for both published studies reporting intra-rater reliability and likely to have acquired familiarity with the atlas images (Menz et al. 2007; Roddy et al. 2015).

Therefore, intra-rater reliability of the researcher (PMc), although considered 'fair' in specific joints of foot OA, did show 'moderate' reliability providing an appropriate level of confidence for future evaluation of radiographic images by the observer, based on a relevant scale categorising the level of agreement. This is comparable to the 'moderate to excellent' levels of intra-rater reliability demonstrated by Menz et al. (2007) and which were documented as being similar across specific joints when using Kappa scorings. It is important however, to mention that scorings appeared to be unspecified in terms of either being a calculation of combined feet for each joint, or being a

calculation of a single foot of each participant in the work of Menz et al. (2007) which likely would have affected the intra-rater reliability for the results of osteoarthritis among joints. Importantly, the research for this chapter was also carried out in the early stages of the MPhil project when the investigator was developing understanding of and knowledge in the use of the atlas (2012).

4.6.2. Appropriateness

The LFA has the potential for some ambiguity in the interpretation of the scoring for osteophytes and joint space narrowing within individual joints. With only dorsoplantar views available within the year 6 Chingford 1000 Women study data to evaluate the natural history of radiographic osteoarthritis (Chapter 6), the results potentially could show an under-estimated value for the population prevalence of radiographic foot osteoarthritis among women. To address this, techniques were established following contact with experienced researchers and clinicians in radiographic diagnostic techniques acknowledging concerns of 'user' limitations or bias of the atlas when evaluating joints for presence of osteoarthritis. These are summarised as follows:

- Exclusion of 'ungradable' joints which cannot be compared with the LFA guidance without using any form of interpretation e.g. tracing bony structures to distinguish a joint (Technique 2: ungradable joints).
- Inclusion of a higher score allocated to joints with uncertainty between two grades for each relevant e.g. Where uncertainty exists over a score of '2' or '3' in either radiographic feature, a score of '3' is awarded (Technique 3: overscoring).

It is important to understand the difference that exists in prevalence of radiographic osteoarthritis in the feet between established and over-scoring methods whilst using the LFA. Through comparison of the techniques, it is understood that greater variation exists between radiographic projections and joints in revised techniques 2 and 3 compared to established methods. This reduces confidence for the over-scoring method, however it does provide the important evidence and context for the number of joints, feet, or people where osteoarthritis may exist but is not diagnosed due to ambiguity in applying the atlas to the individual clinical x-rays. Furthermore, it is more appropriate to underestimate disease burden through prevalence to ensure better confidence in confirmed cases.

Using the revised technique, technique 2 (ungradable joints), it was evident that inclusion of 'ungradable' joints that are given a score in technique 1, as stated in the LFA, increase the prevalence of OA. This was an important investigation for understanding a potentially more 'true' prevalence that exists, that is, joints diagnosed with absolute certainty of accuracy by the user of the

atlas. It shows the potential for the margin of error and the difference of 6.4% shows the possible difference resulting from ambiguity in joint evaluations in the study population that gives an underestimation of 'true' radiographic OA.

4.6.3. Validity

The LFA has been used to determine prevalence of foot osteoarthritis in various research studies (Menz et al. 2007; Zammit et al. 2008; Menz et al. 2009; Roddy et al. 2015). Prior to this, according to Trivedi et al. (2010), the Kellgren and Lawrence approach had previously dominated. The LFA scoring method is, however, based on the principles adopted by the Kellgren and Lawrence atlas for grading osteophytes and joint space narrowing (Kellgren & Lawrence 1958) and osteoarthritis is scored on both feet in two radiographic views (dorsoplantar and lateral). According to the LFA authors, the purpose of the lateral projection (additional to dorsoplantar) ensures there is an appropriate level of sensitivity to osteoarthritis (Menz et al 2007). The two projections were also identified as the gold standard in evaluating radiographic osteoarthritis (Menz et al. 2009). The availability of only one radiographic view, the dorsoplantar view, in the year 6 Chingford 1000 Women study data was considered as a limitation that could affect the reliability of results in the main investigations of prevalence (Chapter 5) and incidence of foot osteoarthritis (Chapter 6).

The low prevalence of joints graded '2' or '3' (presence of OA) shown, with the exception of the 2nd CMJ in joint space narrowing (both feet and both projections) and the 1st CMJ osteophytes (both feet in the dorsoplantar projection) was particularly interesting. This aligns with the work by Menz et al. (2007). Menz et al. (2007) discussed features among joints, 1st CMJ osteophytes only in the dorsoplantar projection and 2nd CMJ space narrowing, which demonstrated low scores in inter-examiner reliability. This strengthens the case for comparability between studies and validates the work by Menz et al. (2007) using the Chingford 1000 women study. Important to this study was the consideration of the gender specific approach to the analysis. Menz et al. (2007) described women as having a higher median number of joints affected than men. This gives us an insight into differences that exist between men and women, most notably the higher number of osteoarthritic joints among individual women. However, it is not known if the number of women affected by radiographic foot osteoarthritis (disease prevalence in a population) differs to men.

The high prevalence of low grades (absence of OA) and low prevalence of high grades (presence of OA) suggests that, certainly for the dorsoplantar view, there has been a tendency to grade in the non-present grades of radiographic osteoarthritis rather than the present grades of radiographic osteoarthritis. This is further supported by the fact that the atlas is established as being reliable and

valid and the general pattern across all joints shows a generally higher prevalence in non-present grades of radiographic osteoarthritis (Roddy et al. 2015).

In identifying the established method as the better measure of radiographic osteoarthritis, combined projections have been identified as the best approach and in scenarios permitting only one projection, the dorsoplantar should be used. Findings from this study indicate that the effect of combining both dorsoplantar and lateral views reduces the number of ungradable joints. With only the dorsoplantar view it is possible that the prevalence of foot osteoarthritis could be underestimated however the dorsoplantar view was identified as the most appropriate view where only one view can is available in the analysis (Chapter 4).

This study is difficult to compare to other studies of its kind as basic epidemiological work on radiographic osteoarthritis is limited at best in its own right. Roddy et al. (2013) however, established high scores in intra-rater reliability achieving excellent scores yet inter-rater reliability was moderate. Having demonstrated the fact that the atlas is open to interpretation in various ways, this, along with the results of the CASF study, would suggest that perhaps those evaluating x-rays in the study are confident with scoring but use differing techniques.

4.7. Strengths and potential limitations

The strengths of this study are:

- Reliability of the observer and within the study participants established
- Reliability was assessed early in the MPhil project when the MPhil student had less experience at scoring x-rays and yet established as acceptable for subsequent work.
- Different techniques to analyse reliability which account for limitations of the LFA which have not been tested before.
- The identification of the dorsoplantar projection as the more reliable method when only one view is available provides justification for study 3 which only had availability of the dorsoplantar projection x-rays.

Several potential procedural limitations need to be considered in light of the results produced.

1. *Quality of year 6 foot radiographs*

The foot radiographs used to test intra-rater reliability were taken at the year six assessments for the Chingford 1000 Women study. All were taken semi-weight bearing, as opposed to weight bearing as stated within the LFA. This could affect the quality of the acquired image, and therefore subsequent interpretation. The gold standard for radiographic imaging of the lower limb has been identified as a fully weight bearing procedure (Mandi & Mandracchia 2008).

The year 6 radiographs were 17 years old and although x-rays of the knee in the Chingford 1000 women study demonstrated some deterioration when used in previous research, the storage of the x-rays differed between the knees and feet. The foot x-rays were more appropriately stored as they were individually filed in opaque envelopes impenetrable by sunlight and for the most part stored in a dark storeroom. Additionally, the x-rays were captured using high quality film and there was no observable deterioration, therefore it unlikely that the integrity of the films was affected.

When comparing the radiographs using the LFA atlas, it is likely that x-ray machines with higher specifications were used for the development of the LFA compared to the images taken in year 6 of the Chingford study. This raises an issue in itself given that physical films are being compared with higher resolution digitised images. Images were compared using a printed version of the LFA atlas rather than using a PDF viewed on a computer monitor which may account for this unusual disparity (considering long term exposure during evaluation period) between the assessed and standard atlas images.

2. *Clarity of scoring*

The authors of the LFA have stated that severe forms of structural foot osteoarthritis are more likely to be present in both radiographic projections than mild or moderate forms of osteoarthritis (Menz et al 2007). Using only the dorsoplantar projection may have affected the sensitivity to detect mild or moderate forms of structural changes consistent with OA. The learning process involved in scoring the radiographic images from the year 6 data may have influenced scoring. Reliability work took place at the beginning of the researcher's MPhil and training in the scoring of foot radiographs. This may have resulted in the reliability of the results being lower.

Of note, difficulty arose when the experience of the researcher (PMc) was novice level and there was an over reliance on the LFA pictures for interpretation and radiographic appreciation of the individual foot joints. This may have affected reliability of the scoring during the initial phases of the reliability work. This issue was reviewed through further training and consensus with the supervisory team. From this further training revised techniques (techniques 2 and 3) were devised to validate the researcher's technique on the larger dataset of foot radiographs.

The cohort used in the development of the LFA was a sample of the Australian population over the age of 65 years. The Chingford study participants at year 6 (from baseline) were aged 49 to 65 years old and at year '23' the participants were aged 69-93. The difference in age of the cohorts may have affected reliability in the researcher's scoring technique as the pictures that align with the scoring method in the LFA may not be representative of the Chingford 1000 Women study cohort.

4.8. Conclusion

In order to ensure robust results in identifying radiographic foot OA, three key areas of feasibility in relation to the collection of data were investigated; reliability, validity and appropriateness.

Intra-rater reliability demonstrated 'fair' and 'moderate' reliability in diagnosing radiographic foot osteoarthritis when evaluated by the researcher (PMc). Limitations were noted that may have reduced reliability in the use of the LFA scoring method for use in an established sample. However, the limitations were considered resulting in a revised technique to further explore the validity of using the LFA to determine foot osteoarthritis in the established Chingford 1000 Women study data. Despite the exploration of other techniques or methods, it was established that the most favourable method was the technique advised by the authors of the LFA; furthermore, where only one projection is available, the dorsoplantar projection could be relied upon to enable scoring for an estimate of presence of radiographic foot OA.

4.8.1 Key Points

Feasibility using the LFA

Key points

- Reliability, validity and appropriateness were all determined within the study.
- Reproducibility was established through intra-rater reliability of the observer which was considered to be acceptable.
- Revised grading methods were agreed through consensus to consider reliability of the results produced whilst using radiographic foot atlas. Which established Technique 1 as the most valid and accurate approach.
- Using both radiographic projections is better for appropriateness but the dorsoplantar is more appropriate than the lateral where only one projection is available.
- Despite its recognised limitations, the established method of evaluating joints for radiographic osteoarthritis is the best on the condition the results are interpreted with caution.

4.8.2 Summary

The outcome of the investigations in this chapter is that the use of the LFA can be considered feasible in identifying radiographic foot osteoarthritis in the Chingford 1000 Women study. The core concepts of feasibility; reliability, validity and appropriateness have been clearly demonstrated in this study with reliability of the observer using a scoring atlas established, the appropriateness of one radiographic projection with the atlas, and best scoring technique established whilst using the atlas. Prevalence estimates and ranges of error have been presented that provide the foundation to the subsequent chapters in this thesis (five and six) identifying prevalence of radiographic osteoarthritis (study 2) and the natural history of radiographic foot osteoarthritis (study 3). In addition to this, study 2 and study 3 will also present data on prevalence and natural history of foot pain respectively, whilst also presenting co-existence with radiographic foot osteoarthritis.

Chapter 5: Study 2 – Prevalence of radiographic foot osteoarthritis and foot pain.

5.0. Introductory chapter summary

This chapter considers prevalence and distribution of radiographic foot osteoarthritis and foot pain in detail, using a number of different variables and stratifying prevalence according to key characteristics in osteoarthritis. The aims and objective are defined, methods are outlined and results presented, and key themes and points are discussed; with conclusions provided at the end of the chapter.

5.1. Introduction

Work in the previous chapter determined the presence of radiographic foot osteoarthritis and investigated the reliability and validity of a scoring method using the LFA (Menz et al. 2007) to establish this. Chapter 4 thus provided a prevalence estimate of radiographic foot osteoarthritis at the person level (91.3%) and at the joint level. The clinical relevance of structural changes due to osteoarthritis without consideration of pain symptoms is, however, often questioned in the published evidence (Hadler 1992).

It is understood from investigation into osteoarthritis of other joint sites that associations between structural change and pain have, at best, a weak association (Zhang and Jordan 2010). However, Hadler (1992) considered a novel attitude in understanding osteoarthritis within a context of pain. Hadler stated that knee pain is the 'malady', rather than osteoarthritis, thereby suggesting that the focus of research has been inappropriate. He also alluded to physicians often assuming a relationship whereby the process of structural change in osteoarthritis is reflective of the pain experience. This was illustrated by describing a typical patient presentation of knee pain and the observation of osteophytic change using radiographic imaging.

Foot pain is complex and has a multifactorial influence on how it is perceived by each individual person (Thomas et al. 2004). In Chapter 2 (sections 2.10. and 2.11.), pain was highlighted as an important and relevant variable to investigate; exploring if relationships are established between the experience of pain and pathophysiological processes. In the case of radiographic foot osteoarthritis, the relationship with foot pain is not well established and the most comparable research relates to participants recruited according to symptoms (Roddy et al. 2015). Pain data can be collected using various methods, therefore to ensure comparability between existing and novel data it is important that the investigation of such relationships is carried out with consideration to a variety of methods

of obtaining pain data. Existing evidence focuses on patient self-reported pain and there appears to be little or no evidence of clinician diagnosed pain and the frequency with which clinicians can expect to encounter it in patients (Roddy et al. 2015). This, along with the more commonly presented self-reported foot pain data, are important considerations when carrying out further prevalence work in radiographic osteoarthritis. Although work has considered the prevalence of foot osteoarthritis where there is already a related pain experience, no studies have considered the prevalence in a general population; which may include individuals with symptomatic or asymptomatic osteoarthritis.

This chapter explores the presence of radiographic foot osteoarthritis and its co-existence with foot pain. This will involve looking at patterns and dispersion of radiographic osteoarthritis and pain in the foot, in combination and individually. These data should provide novel research that has not been detailed to this level before.

RESEARCH QUESTION

What is the prevalence of radiographic foot osteoarthritis and co-existing foot pain in a UK population-based cohort of older women?

5.2. Study aims and objectives

Aim: Investigate and describe the prevalence and distribution of radiographic osteoarthritis occurring within the foot and co-existing foot pain in a UK population-based cohort of older women.

Objectives:

- Define the prevalence, severity and distribution of radiographic osteoarthritis in the foot among a UK population-based cohort of older women.
- Characterise the prevalence of foot pain among older women from a UK population-based cohort using different pain parameters.
- Define the prevalence of radiographic foot osteoarthritis with co-existing foot pain among older women.

5.3. Methods

5.3.1. Participant recruitment

In this study, participants were sourced from those participating in the Chingford 1000 Women study. This group, which was representative of the UK population of older women, were returning for their year '23' clinical visit.

All participants still active within the Chingford 1000 Women study were sent a letter of invitation and a participant information sheet by post. These described the study protocol and their proposed involvement. Potential participants who were willing to be considered for the study were given the opportunity to discuss the details of the study with the research assistant for the site (Maxine Daniels), or the chief investigator (Nigel Arden). Those individuals who were willing to take part in the study were given an appointment to attend for clinical assessment and an appointment for foot x-rays to be taken. At the start of the clinical visit, the study protocol was explained in detail by the chief investigator and participants were encouraged to ask further questions before deciding to sign the form of consent. All willing participants were given a copy of the participant information sheet and a copy of their signed consent form to keep (Appendix 5). Once informed consent was obtained, patients were screened for acceptance onto the study. Research staff included the MPhil student (Peter McQueen) who is a HCPC Registered Podiatrist, the research assistant (Maxine Daniels) and a registered nurse and phlebotomist (Eileen Salman) who were based at the Silverthorne Medical Centre in Chingford.

5.3.2. Data Collection

Data collection for the Chingford 1000 Women study year '23' clinical visits took place between November 2013 and July 2015. Analysis of the data took place between July 2015 and September

2016. Clinical visits involved the use of IMFAA (see appendix 14) to collect a number of different variables reliably (Gates et al. 2015).

5.3.3. Location

All clinical foot and ankle assessments took place during a single appointment at the Silverthorne Medical Centre, Chingford. On each occasion, the same consultation rooms and facilities were utilised in an attempt to standardize environmental factors, such as room temperature. Whilst the preliminary examination was conducted, action was taken to preserve the patient's dignity at all times, in line with ethical guidelines.

Data collection for foot x-rays took place, initially at InHealth's NHS Stratford site. Due to a change in contract, foot x-ray visits were transferred to Holly House Private Hospital in Chigwell. A standard operating procedure for foot x-rays had been drawn up *a priori* and for both radiography sites meetings were held with the radiographers to ensure minimal deviation from the protocol.

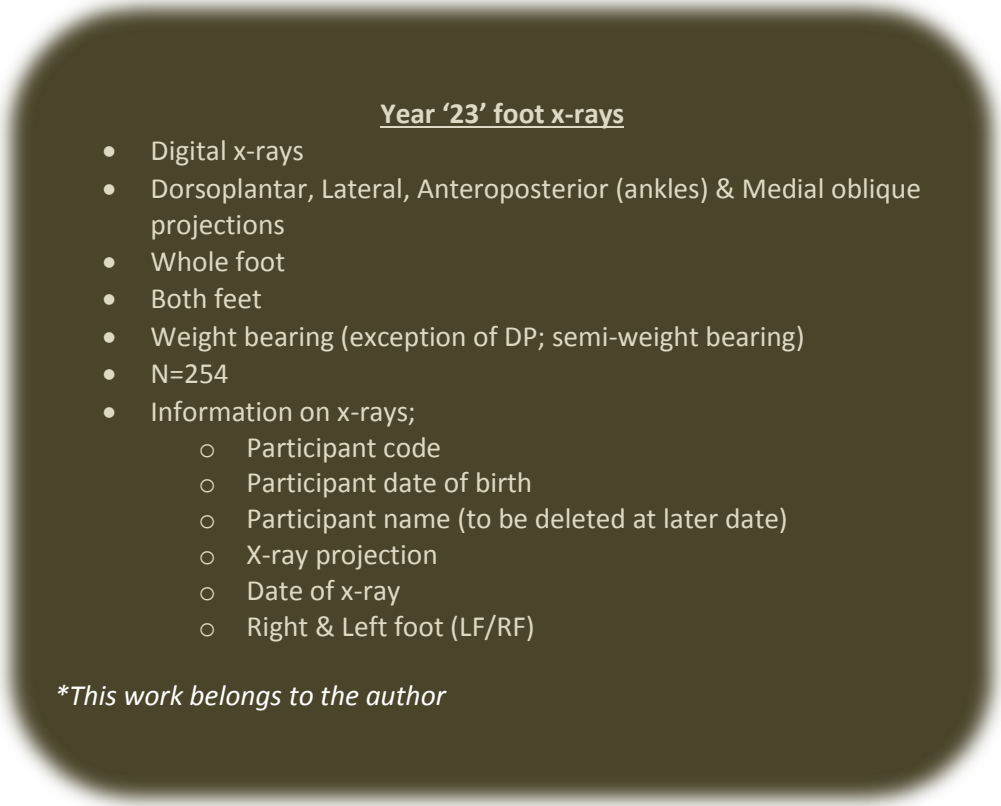
5.3.4. Study design

This study made use of the 'Chingford 1000 Women study' based in North London where participants with no known pathology were recruited as part of a prospective study in 1989. The study focussed on cross-sectional observations using a longitudinal prospective cohort study. Year '23' was the first year to consider foot characteristics although, of note, year 6 captured radiographic imaging of the foot and related variables were also collected historically.

The study focused on classifying osteoarthritis in pathological terms using diagnostic imaging, more specifically, radiographic imaging. Prevalence, severity and distribution were presented using year '23' x-ray data where two radiographic views were available. year '23' foot x-rays were evaluated for osteoarthritis using methods for establishing the best technique as discussed in Chapter 4.

The standard operating procedure for year '23' is summarised in the key facts infographic (Figure 10). year '23' x-rays were used to establish the intra-rater reliability in the radiographic appreciation of foot osteoarthritis among the study population. The focus of Chapter 4 was to consider the reliability of the observer at key points throughout the evaluation of x-rays and the difference in methods of evaluation using the LFA. The validity and reliability of the LFA as a radiographic scoring atlas (study 1, chapter 4) has therefore been established for use in investigating the prevalence of radiographic foot osteoarthritis in study 2 (chapter 5).

Figure 10 Summary of the foot x-ray protocol at year '23'



5.2.4.1. Selection criteria

All participants still active within the Chingford 1000 Women study were considered appropriate for this study.

Inclusion criteria

- Women registered with the Chingford 1000 Women study
- Aged 40 and above

Exclusion Criteria

- Individuals too physically unwell to attend
- Individuals who were deceased or had withdrawn from the Chingford 1000 Women study
- Individuals unable to attend for other reasons

Key reasons for exclusion from analysis included the inability to distinguish left and right feet on x-ray and participants who attended the clinical appointment but did not attend x-ray.

The question of whether or not inflammatory joint conditions should be excluded from the analysis was discussed. A simple analysis of the year '23' cohort was carried out to establish prevalence of inflammatory arthritis which showed a prevalence of 25.6% (75; 293). This compares to the 22.7% of the US population reported to have any kind of physician diagnosed arthritis (Hootman and Helmick 2006). There are several considerations that need to be made in light of this information. Information on the prevalence of inflammatory arthritis is limited, and so there was a distinct lack of information on which to inform the decision to either include or exclude participants with inflammatory arthritic joint conditions. The population of the referenced research is an American population, whereas the Chingford cohort is UK based and prevalence may therefore differ due to pathophysiological differences (an accepted limitation when making comparisons). Although American study participants were also selected from the general population and both genders were considered in the study investigation resulting in an likely lower prevalence of arthritis compared with the cohort of Chingford study participants, age is importantly not considered to be a predictive characteristic in inflammatory joint conditions (Gibofsky 2012).

However, this prevalence was also inclusive of osteoarthritis, which is likely to inflate the prevalence in the study given the presence of inflammatory markers, as described by Barbour and Cauley (2013). Participants were also physician-diagnosed, where it was self-reported arthritis that was identified among the Chingford participants. This suggests that there may have been misdiagnoses, resulting in the increase of the prevalence among Chingford participants.

In the 'CASF' study led by Roddy et al. (2013), of 560 participants, 24 were identified as having inflammatory arthritis and were consequently excluded. Whilst this seems a particularly low prevalence and no understanding of the selection of such participants was provided, it is important as a consideration. The 4.6% prevalence of inflammatory arthritis differs by a notable degree of 21.0% from those identified in the self-reported inflammatory arthritis of the Chingford based women.

Further to this, anecdotally, additional data collected for a smaller cohort study by the University of East London demonstrated lower trends of inflammatory joint conditions when participants were questioned as to whether they had been given a professional diagnosis. There was also strong evidence in the questioning of participants that some participants struggled with health literacy. In light of these considerations, the prevalence of inflammatory joint conditions appeared not to be reflective of the general population, irrespective of the higher age group and female gender of

participants. Therefore it would not be appropriate to exclude participants, particularly from an epidemiological stand point, when attempting to capture population prevalence. The likelihood is that this could result in a biased result of under-representative prevalence due to the known association between osteoarthritis and inflammatory joint conditions (Gibofsky 2012). Further to this point, if these participants are excluded, there is the possibility the data may fail to demonstrate a representative sample and result in the data losing the generalisability to this age group of the population.

5.3.5. Assessment of demographic and clinical characteristics

At the clinical visits, general demographic data including age, weight, height and limb dominance were recorded. Clinical data including clinician diagnosed pain at specific sites were also collected. Table 14 summarises relevant information about these variables. Additional variables were collected with a view to investing in future research following the work presented in the thesis. These additional variables can be found in Appendix 16.

Table 14 Core variables including in clinical data collection

Core measure	Source	Reference	Justification
Age	N/A	N/A	This is a key variable required when considering natural history in order to present the natural history of pain and of osteoarthritis as with preceding research in other sites (Leyland et al. 2012; Franklin et al. 2011).
Weight	N/A	N/A	These are important population characteristics to present in a study on pain and osteoarthritis in the foot as with previous studies in this area (Roddy et al. 2015; Menz et al. 2007; Wilder et al. 2003).
Height	N/A	N/A	
Limb dominance*	N/A	Velotta et al. (2011)	Limb dominance was collected with the intention to consider co-existing prevalence with osteoarthritis to support the discussion on prevalence of osteoarthritis.
Foot Posture	Foot posture index	Redmond et al. (2001)	Foot posture was an important population characteristic to present in the study to provide an understanding of foot related characteristics.
Clinician diagnosed pain: 1st MTPJ†	Based on IMFAA	Gates et al. (2013)	This was primarily in line with the presentation of the wide range of pain variables within one study cohort and related to specific joints. These variables were a specific insertion to the data collection with the intention to present pain at specific joints.
Clinician diagnosed pain: 1st CMJ†			
Clinician diagnosed pain: 2nd CMJ†			
Clinician diagnosed pain: N1stCJ†			
Clinician diagnosed pain: Ankle†			

**Limb dominance was later found to be an unusable variable*
†Clinician diagnosed pain was later found to have a very low prevalence and therefore was not statistically appropriate.

5.3.6. Assessment of radiographic foot osteoarthritis

In order to establish the prevalence of foot osteoarthritis within this UK population-based cohort of older women, it was necessary to x-ray the feet. There is no alternative means of screening participants with the same validity and reliability for assessing joint condition. The presence of radiographic foot osteoarthritis (rOA) was defined using the LFA definition of one radiographic feature in either projection graded as '2' or higher; as detailed in Chapter 4.

Definition of radiographic foot osteoarthritis:
Osteophytic change or joint space narrowing grade 2 or 3 in any joint (1st metatarsophalangeal joint, 1st cuneo-metatarsal joint, 2nd metatarsophalangeal joint, Navicular 1st cuneiform joint, Talonavicular joint) in either projection (dorsoplantar or lateral).

The procedure for foot x-rays was drawn up by the MPhil student and entailed the following:

1. Foot x-rays were arranged so that they coincided with the clinical visit and clinical foot assessments (ie. on the same day or as close to this as possible).
2. Foot x-rays were taken barefoot.
3. All foot x-rays were taken as a dorsoplantar (DP) view of both feet together, and lateral views carried out for each foot individually (Table 3).
4. All x-rays were taken partially and fully weight-bearing (Table 3).
5. All operators of diagnostic X-ray equipment had experience and training in radiation safety [IR(ME)R 2000 and IRR 1999].
6. The radiographic films were reviewed by a consultant radiologist at the InHealth Stratford NHS radiology unit or Holly House Hospital department of radiology for any radiographic 'red flags' or significant radiographic abnormality.
7. All images were stored using the following code: [participant code], view and image number: for example, 263/DP/10.
8. The radiographic films of both feet were reviewed and scored by the same investigator (PMc) who had extensive training and reliability testing in reading foot x-rays to evaluate the prevalence of osteoarthritis as well as extensive experience in grading the foot x-rays for the Chingford study. The coding framework followed the principles outlined by the LFA (Menz et al. 2007) as determined in Chapter 3.

5.3.7. Assessment of foot pain

Following a review of the literature (see section 2.9. and 2.10. in Chapter 2) it was clear that assessment of foot pain raises some important questions: what characteristics should be considered as important in constituting the experience of foot pain? and, should this be inclusive of 'pain' as an isolated item, or should it encompass 'pain', 'aching' and 'stiffness' as denoted by Hill et al. (2008). Therefore, for assessment of foot pain in this study, it was agreed that three levels of foot pain would be considered: patient reported global foot pain (GFP), patient reported foot specific pain (GenFP) and clinician assessed joint level foot pain (FJP). Questionnaires included self-assessed questions on foot pain using the Manchester Foot Pain and Disability Index (MFPDI) (Garrow et al. 2000) and questions related to the frequency, duration and location of pain.

Different pain variables were collected at year 6 and year '23' and included closed questions and related pain manikins (full body and foot specific), self-reported outcomes and clinician diagnosed

foot pain, as stated below, with the background and data collection methods clarified throughout. In terms of prevalence of foot pain, the primary considerations were generalised foot pain (Gen.FP), global foot pain (GFP) and foot joint pain (FJP). The foot pain data collection method which is considered to be valid and reliable for self-reported foot pain is the Manchester Foot Pain and Disability Index. However, in the context of this study, the key limitation of the index relates to the identification of foot pain whereby specific foot joint pain is not established.

5.3.7.1 Patient reported foot pain using a global pain (GFP) manikin

Single closed questions asking participants about experience of pain in their lifetime and in the past month were:

- *Please state the number of days in the past month that you have experienced pain:……days*
- *Participants were asked to shade the area of any pain experienced on a full body manikin (Figure 11).*

Figure 11 Full body manikin

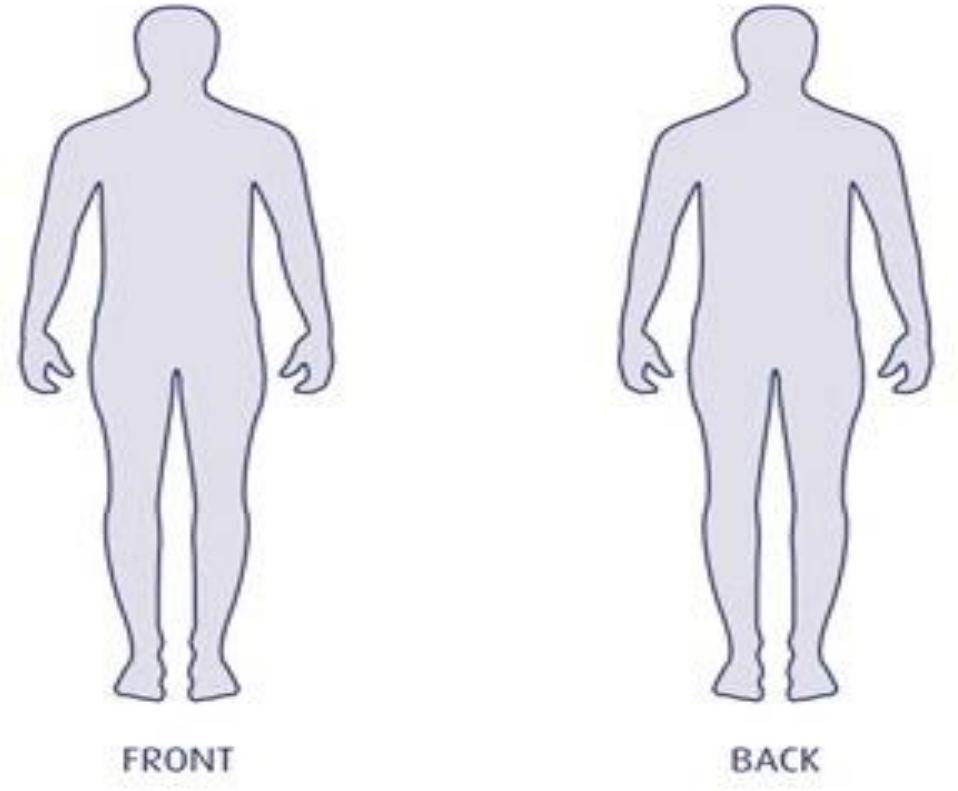
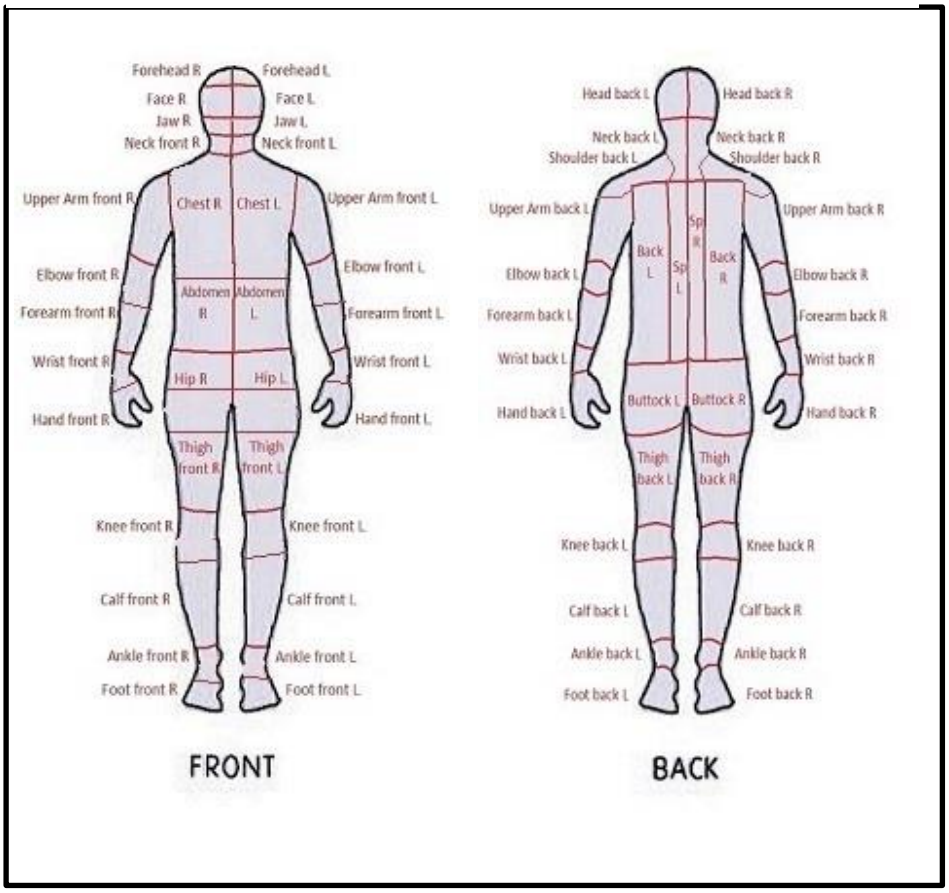


Figure 12 Global pain with reference to the feet



Disabling foot pain was established primarily using the MFPDI (Appendix 8) using differing definitions from current literature. Disabling foot pain (GFP) prevalence is presented in five key formats which can be found in table 2.

5.3.7.2. Closed and single sentence foot pain questions (year '23') (Gen.FP)

The foot manikins included within the MFPDI were used to determine foot specific pain. Questions asked participants about experience of pain in their lifetime and in the past month.

The questionnaires included self-reported questions on foot pain related to the frequency, duration and location of pain. These questions can be viewed in table 15.

Table 15 Pain questions in questionnaires

Closed and single sentence questions on foot pain	Action or response requested of participants
Have you ever had pain in your feet which has lasted one day or longer?	• Positive or negative response (Yes or No) • Shade painful area which corresponds to the foot diagram
If you have had pain in your feet, has it changed over the last 6 years?	• Positive or negative response (Yes or No)
In the past month have you had pain in your feet which has lasted a day or longer?	• Positive or negative response (Yes or No) • Shade painful area which corresponds to the foot diagram
Please state the number of days in the past month that you have experienced pain:……days	• Provide number of days of pain

The participant questionnaire for Chingford year '23' contained a single filter question; ***'In the past month have you had pain in your feet which has lasted a day or longer?'***. This was a shortened, closed question version of the Manchester Foot Pain and Disability Index; ***'For each statement indicate if this has applied to you during the past month. If so, was this only on some days or on most or every day in the past month?'***.

The CASF study used a similar question with the addition of the symptom of aching; ***"In the past month, have you had any ache or pain that has lasted for one day or longer in your feet?"***. Where participants responded positively, the following instructions were given to complete the foot pain manikin (Garrow et al. 2004); ***"Please shade, in the diagrams below, any pain you have had in your feet in the last month that has lasted one day or longer."***

In the Chingford study, participants were provided with the following information; ***'If yes, please shade on the diagram below ALL the places that have been affected',*** followed by the foot pain manikin (Garrow et al. 2004). The foot pain manikin diagrams were sourced from Otter et al. (2010) (used with permission) and the Manchester Foot Pain and Disability Index foot (Garrow et al. 2000) to consider pain according to 25 predetermined sections of the 'upper' (dorsal aspect) and 'lower' (plantar) feet, whereby patients shaded manikin feet according to their pain. The use of dorsal and plantar foot manikins replicates the methods used by Dufour et al. (2009).

Figure 13 MFPDI foot pain diagram - Plantar aspect

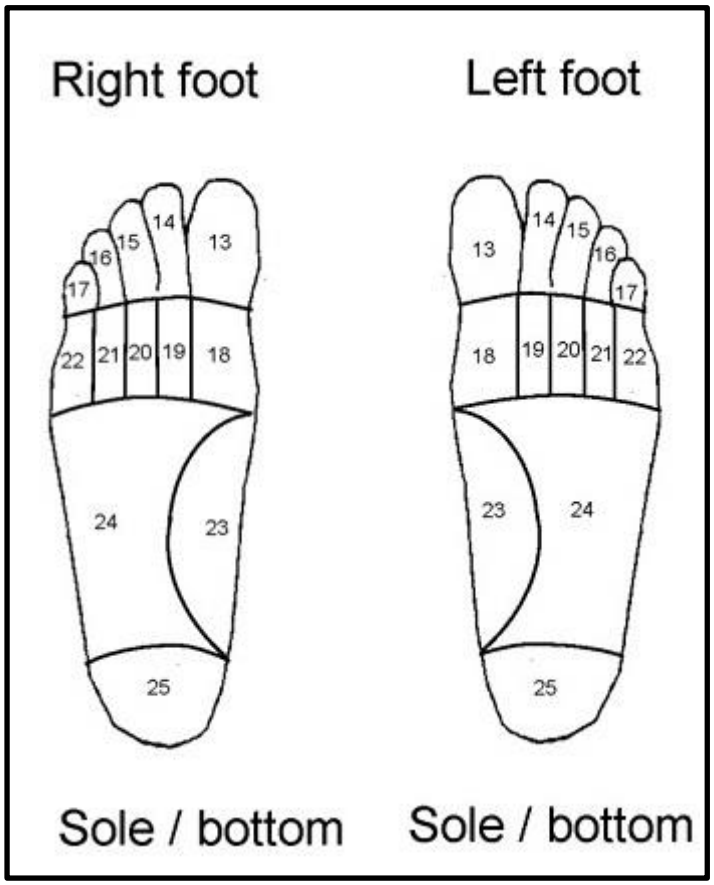
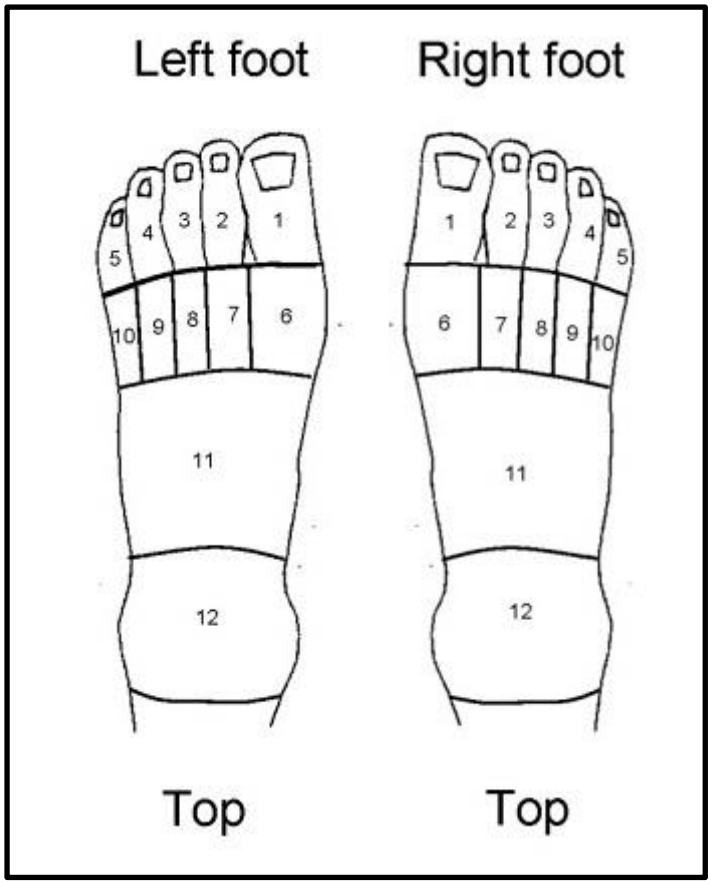


Figure 14 MFPDI foot pain diagram - Dorsal aspect



Key differences between the CASF study and Chingford year '23' study are the inclusion of the symptom 'to ache' and the inclusion of the posterior and anterior views of the feet in the CASF study, which included the ankles. In order to maintain consistency with other research studies, the symptom of 'aching' was disregarded in the Chingford year '23' study. In addition to this, ankle pain manikins were excluded, as the focus of the study was specific to the feet and ankles bore limited relevance within this thesis.

5.3.7.3. Closed and single sentence questions (year 6) (Gen.FP)

The following questions were extracted from the year 6 data collection of the Chingford 1000 Women study. These were answered and recorded as either a negative response, or the left foot, right foot or both feet. The questions asked were;

- 'Left foot: Have you had any episodes of pain, stiffness or swelling in past year?'
- 'Right foot: Have you had any episodes of pain, stiffness or swelling in past year?'

These questions were formulated prior to data collection in 1995 and before the development of standardised and tested pain variables. The source of these is unknown, but it is understood that these variables were developed for the sole purpose of the Chingford 1000 Women study year 6 data collection.

5.3.7.4. Clinician diagnosed foot pain (year '23') (FJP)

Foot pain was diagnosed through palpation of joints with passive range of motion type testing in joints that could be identified with absolute certainty. The 1st metatarsophalangeal, 1st cuneo-metatarsal and talonavicular joints were identified as palpable using range of motion, and all other joints (1st cuneo-metatarsal and navicular 1st cuneiform joints) were considered for bony prominences as a viable alternative to signs and symptoms of osteoarthritis. Clinician assessed foot joint pain was determined during the clinical assessments. The thesis author (PMc), is a Podiatrist experienced in conducting all required assessments, which involved carrying out 'range of motion' or 'dynamic motion' tests and identifying bony prominences where ROM could not be accurately assessed on the following joints:

- 1st metatarsophalangeal joint (ROM)
- 1st cuneo-metatarsal joint (bony prominence)
- 2nd cuneo-metatarsal joint (bony prominence)
- Navicular 1st cuneiform joint (bony prominence)
- Talonavicular joint (ROM)

Participants were asked if they experienced any pain or tenderness in any of the joints while the clinician was moving or palpating the individual joint.

5.3.8. Assessment of disabling foot pain

As Roddy et al. (2013) used a symptomatic population to consider prevalence of radiographic osteoarthritis, foot pain was identified using the MFPDI foot pain manikins (where pain had been experienced in the past four weeks) in regions corresponding to joints with radiographic osteoarthritis. This definition referenced Garrow et al. (2000) as being the original source of the definition whereby participants were required to have foot pain lasting one day or longer in the past month. However, Garrow et al. (2000) did not identify whether this was using a closed question or the MFPDI foot pain manikin. Of note, the later work by Garrow et al. (2004) identified the means of filtering foot pain among participants using the following question, *'Have you experienced foot pain lasting at least one day during the past month?'*. However, unlike the later work by Roddy et al. (2013), this filter question was also used previously by the same author (2011). This may be explained by the fact that the latter population was symptomatic and the need to identify correspondence to joint regions. As this study considers generalised foot pain and disabling foot pain, the traditional (more frequently used) single closed question definition was used to identify foot pain.

Roddy et al. (2009) established that foot problems are common, and therefore when considered as a standalone variable, are not appropriate when considered as a measure of disabling foot pain and means of differentiating from non-disabling foot pain. The authors additionally state that this method of measurement could result in over-estimation of the symptomatic population, as foot problems are not necessarily symptomatic. It was also established by the authors that better reliability existed when incorporating at least one item from the MFPDI function constructs (on most/every day) with the preceding filter question to initially establish foot pain (Roddy et al. 2009). However, the research by Roddy et al. (2013) referenced the definition from earlier in 2009, also by Roddy et al., where the ten item functional definition was used, although this appears to be inconsistent between papers using the definition of disabling foot pain. Notably the earlier paper in 2009 made use of all 17 items of the MFPDI in defining disabling foot pain.

A limitation that has emerged relates to the lack of clarity in identifying which items of the MFPDI were used to define disabling foot pain in the research by Roddy et al. (2013). Uncertainty was between two possible methods, the ten item 'functional problems' (Garrow et al. 2000) which was also referred to in later work by Garrow et al. (2004) and not to be confused with the 'ambulation

scale' of the 'Functional Limitation Profile Questionnaire' of the earlier work (Garrow et al. 2000) or the seven item 'function construct' identified by Menz et al. (2006) through a principal components analysis. Difficulty in identifying which items were used in the research by Roddy et al. (2009) was due to the missing information detailing specific items used to differentiate between defining foot pain and disabling foot pain. On further inspection, research by Garrow et al. (2000) was referenced as the selected method with the 'function' component (1 to 10 of appendix 10) being incorporated into defining disabling foot pain (it should be noted that the MFPDI-17 questionnaire does not correspond to the constructs identified by Garrow et al. (2000). This method was also used in the later work by Roddy et al. (2013) and was shown to achieve a repeatable and valid measure of disabling foot pain in older populations (Roddy et al. 2015). This definition of foot pain was supported by Menz et al. (2011) who investigated different methods and concluded that the definition by Roddy was the most conservative in prevalence and therefore the most appropriate for use in epidemiological studies. The method was also employed by Roddy (2015) in the CASF study, with the aforementioned filter question, and one MFPDI functional item ticked for 'most/every day(s)' if either or both feet were affected.

The MFPDI-19 was used for later versions of the questionnaires, with the MFPDI-17 either being used alone or included as part of the MFPDI-19. The omission of items 18 and 19 of the MFPDI-19 are one aspect that all authors appear to agree on as it has limited relevance in older populations and the MFPDI-17 is a more reliable tool with better construct validity (Garrow et al. 2000; Garrow et al. 2004; Cook et al. 2007; Menz et al. 2006).

Also important are the population characteristics of, and methods identified for, disabling foot pain research. Review of the literature for this thesis has established that disabling foot pain is often discussed as a prevalence in symptomatic populations with pain, and the only clear definition in research relating to disabling foot pain is by Mickle et al. (2011). Five key definitions identified the definitions that exist within the literature which was explored in relation to the Chingford cohort. Therefore, data were presented to clearly demonstrate the prevalence of disabling foot pain without selection of symptomatic or asymptomatic cases from a population. All versions that were extracted from the literature and incorporated into the study are summarised in table 16.

Table 16 Types of Disabling Foot Pain from literature

No.	Part of MFPDI	Item selection	Additional condition
1.	Full tool (17 items)	'On some days' or 'On most/every day(s)'	N/A
2.	Full tool (17 items)	'On most/every day(s)'	N/A
3.	Functional section (10 items)	'On most/every day(s)'	N/A
4.	Functional section (10 items)	'On some days' or 'On most/every day(s)'	Closed question; *In the past month have you had pain in your feet which has lasted one day or longer*?
5.	Functional section (10 items)	'On most/every day(s)'	Any area shaded on either MFPDI foot manikin in either view

5.3.9. Assessment of the co-existence of radiographic osteoarthritis and foot pain, and disabling foot pain

The co-existence with radiographic osteoarthritis primarily considered generalised foot pain, with disabling foot pain and also with clinician diagnosed foot pain. In order to do this, the foot pain manikin suggested by Garrow et al. (2004) for measuring foot pain which was used in the CASF study was used to consider foot pain and disabling foot pain using differing methods as described in the previous sections. As clinician diagnosed foot pain remains under-researched, the co-existence of clinician diagnosed foot pain was also determined according to the statistical power established in section 5.4.2. relating to generalised foot pain. As a result it was established that statistical power could not be adequately achieved and associations between foot pain and radiographic osteoarthritis could therefore not be considered. In addition, the sample size of foot pain established through clinician diagnosed foot pain was so small that it was difficult to establish meaningful discussion of specific results of clinician diagnosed foot pain as a standalone variable.

5.3.10. Revisions to foot pain manikin variables for shading of foot pain (year '23')

As part of the Chingford year '23' visit, revisions were made to data collection questionnaires with input from the MPhil student and research team. The MPhil student requested revisions to two participant self-reported pain diagrams to improve quality of data collection, the full body manikin and the foot pain manikin featured in version three of the questionnaires (table 17). These diagrams were more consistent with the current body of research.

Table 17 Number of pain diagrams completed according to versions of questionnaires

	Generalised pain manikin		Local foot pain	
Live versions* (N=315)	Footless diagram	Full body diagram	UoB diagram	MFPDI diagram
2 (n=118) November 2013	✓		✓	
3 (n=72) April 2014		✓		✓
4 (n=125) July 2015		✓		✓

**Version 1 questionnaire did not go live at any point.*

Version 2 was the first live version of the Chingford based study which had been developed by the ELFOAB project senior researchers and managing team at the University of Oxford. As the ethics application was well underway with the team prior to the MPhil student starting, there was no opportunity for changes prior to the initial ethics submission. This was primarily due to the time pressures of completing data collection in respect of the MPhil timeline. The need for more focused data recognised by the thesis author resulted in prompting other staff who agreed to the changes, creating an opportunity to reconsider variables that had initially been included for the foot manikin. As version 2 made use of a pain manikin of the full body whilst excluding the foot, it was clear that this would provide little additional burden on the participants but provide useful additional data for the MPhil studies and a more 'complete' variable, benefitting the year '23' pool of epidemiological data.

Figure 15 Otter et al. (2010) demarcated foot pain diagram - dorsal

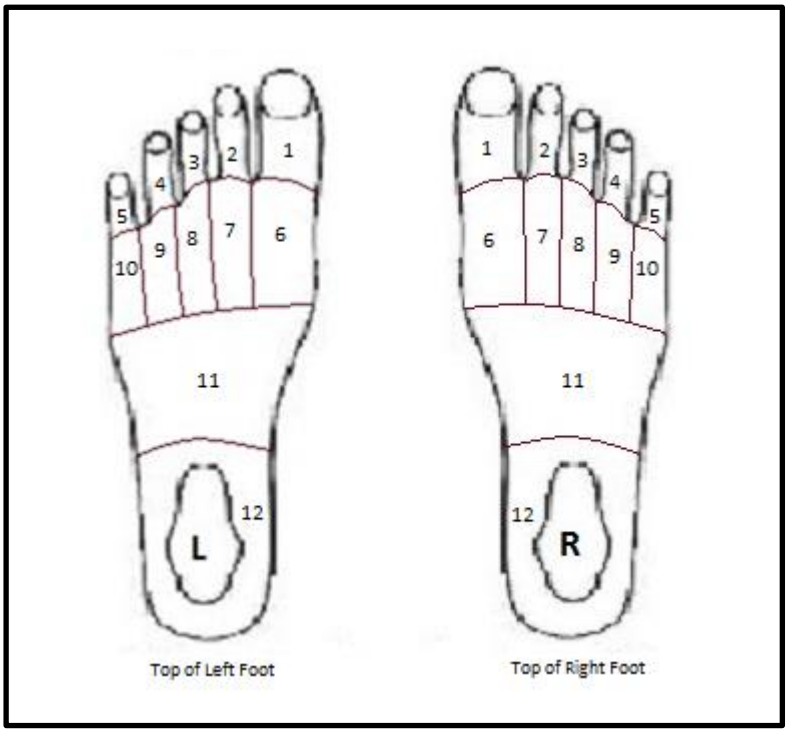
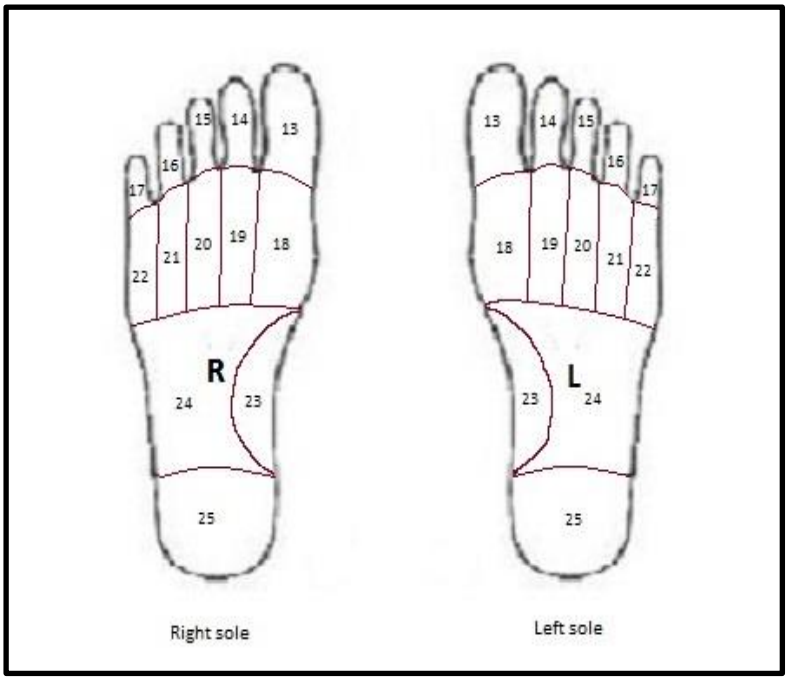


Figure 16 Otter et al. (2010) demarcated foot pain diagram - plantar



5.4. Statistical Analysis

Data from the 'Chingford Women Study' are maintained in an 'Access' database (Access 2000, Microsoft Office). Study data for year '23' were collected and managed using REDCap (Research Electronic Data Capture) hosted at the University of Oxford. REDCap is a secure, web-based application designed to support data capture for research studies. Data were collected and entered into IBM SPSS 22.0 Chicago software to produce the tables and graphs presented throughout the chapter, showing different presentations of the data collected on radiographic foot osteoarthritis and foot pain, individually and combined. All work carried out was observational, providing descriptive statistics. This was detailed through presenting the prevalence of radiographic foot osteoarthritis, foot pain and their co-existence. Radiographic foot osteoarthritis and foot pain were each stratified according to the parameters and accepted categorisations of body mass index (BMI), and of five year intervals of age. This was primarily to understand if any recognisable patterns of disease involvement existed in areas known to affect both pain and osteoarthritis (Munteanu et al. 2012). In addition to this, the prevalence of osteoarthritis and of foot pain was presented according to the distribution prevalence at each joint and rank order to describe the epidemiological themes in a manner representative of epidemiological concepts (Silman & Macfarlane 2002 p35).

5.4.1. Descriptive population characteristics

Basic background demographics were presented among the responders and non-responders at year '23'. Non-responders were identified using data from participants who attended Year 20 but failed to attend at year '23'. However, it was particularly important to consider if there were statistically significant differences at year '23' between those who attended x-ray and those who didn't, as x-ray non-responders were included in the presentation of foot pain data. If statistically significant differences existed, this would show that the data presented in radiographic osteoarthritis and that presented in foot pain are biased by the demographic variable being tested. Variables that were analysed for statistical differences included age, height, weight and BMI as with other similar studies (Roddy et al. 2015; Munteanu et al. 2012). All characteristics were collected with the exception of BMI which was calculated using the following formula;

$$\textbf{BMI} = \frac{\textbf{Weight}^2\ (\text{Kg})}{\textbf{Height}^2\ (\text{m})}$$

To compare responders and non-responders to x-ray using the participants who attended the clinical visit, data were analysed to understand any differences that may bias results. Data were summarised using graphs in SPSS to establish how the data were distributed before identifying the appropriate test to compare datasets for each variable. The patterns were described and compared with current

findings in foot osteoarthritis and foot pain. Prevalence is presented as a percentage. Radiographic foot osteoarthritis was dichotomised where a prevalence of osteoarthritis was required. All foot pain and disabling foot pain was dichotomised to create one variable with binary data. The data used were non-parametric and categorised as nominal. The exception to this was where individual scores using the LFA were used in the presentation of data, meaning data were ordered categorical data. rOA in the foot, foot pain *and* co-existing radiographic foot osteoarthritis and foot pain were stratified according to age and BMI to explore any patterns using the cross-tabulations function on SPSS.

5.4.2. Sample size calculation

Finally, a sample size was acquired with the aim of ensuring a reasonable chance of detecting significant differences (Bowling 2009). Calculating the sample size ensured that statistical power of the results could be achieved and thus provide meaningful results. The sample size was calculated using the following equation:

$$n = \frac{Z^2_{\frac{a}{2}}\, p(1-p)}{d^2}$$

p = proportion of interest

z = confidence level

d = margin of error

a = confidence interval

The sample size required to achieve power was established as 181 participants based on a sample of 557 from the reference population (Roddy et al. 2015). This sample size was achieved using a 5% confidence interval (margin of error) with a confidence level of 95%. Having established a population of 218 participants who attended x-ray, this population is an appropriate size to establish statistical power of the results.

5.5. Results

The analyses focused on:

1. Analysis of the sample background demographics and clinical characteristics
2. Description of the prevalence of radiographic foot osteoarthritis (rOA)
3. Description of the prevalence of foot pain.
4. Description of the co-existence of radiographic osteoarthritis and foot pain

5.5.1. Response rate

The cross-sectional study represents year '23' of the prospective cohort study known as the Chingford 1000 Women study. The response rate at year '23' was 332 participants who attended the clinical appointment and 254 who attended for foot x-ray. Figure 3 provides context to the final numbers who attended clinic and x-rays, those lost to follow-up and those who passed away. year '23' shows a return rate from the previous visit (three years prior) of 64.3%. It is important to consider that the cohort is an older aged group and that a significant time period lapsed between visits for this longitudinal study when considering any response rate or bias. The response rate of returning participants for the Chingford year '23' study was based on the previous data collection point (Year 20) (or 33.1% based on the baseline attendance).

In summary, data were collected from 332 participants. Of the total number of participants, 218 participants were evaluated for changes consistent with foot osteoarthritis and 315 returned the questionnaires on foot pain. However, not all participants completed all sections regarding foot pain (Figure 13, 14, 15 and 16).

5.5.2. Participant demographic

In order to understand the study participant characteristics from which this sample was drawn, demographic data from Year 20 are presented below in table 18 to describe the non-responders at year '23', and demographics of the responders to the clinical visit are presented in table 19.

Table 18 Demographic & clinical variables – Descriptive statistics – year '23'

	NON-RESPONDERS OF YR '23' TAKEN FROM YR 20 (N=115)			**RESPONDERS IN YR '23' (N=331)**		
	Mean (SD)	Range	Total	Mean (SD)	Range	Total
Age (yrs)	69.9* (5.0)	62-84	*n=115*	75.5 (5.1)	68-90	*n=328*
Height (m)	159.6 (6.2)	143-177	*n=106*	158.4 (6.1)	141-177	*n=331*
Weight (kg)	69.0 (13.8)	43.3-112.3	*n=106*	69.2 (12.6)	39.9-113.0	*n=331*
BMI	27.2 (5.1)	18.0-43.3	*n=106*	27.6 (4.75)	17.0-44.1	*n=331*
FPI	Not collected	Not collected	*N/A*	(+)5.1 (3.4)	(-)9-(+)12	*n=329*

**As data were collected around four years earlier, it was expected that participants would be considerably younger*

Table 19 year '23' demographical characteristics of participants

	RESPONDERS N=331 (%)
Gender – female *n=331*	331 (100)
Employed or carer *n=331*	34 (10.3)
Retired *n=331*	287 (85.9)
Housewife *n=331*	45 (13.6)
Other* *n=331*	7 (2.1)
Smoking *n=328*	10 (3.0)
Currently seeing a 'podiatrist' or 'chiropodist' for foot problems (SR) *n=251*	63 (25.1)
Ever seen a podiatrist for foot problems (SR) *n=262*	58 (33.7)
Current use of insoles/orthoses (SR) *n=262*	49 (18.7)
Corticosteroid injection in foot ever *n=262*	18 (6.9)
Surgical intervention in foot ever *n=262*	43 (16.4)
Presence of hand joint nodes (SR) *n=212*	146 (68.9)

**Unemployed (n=1), disability benefit (n=6). Multiple answer question, total boxes ticked N=373) (see cross-tabulations table 28). †Self-reported (SR)*

Using Chi squared analyses for non-parametric categorical data, there were no significant differences in terms of age, height, weight or BMI between responders and non-responders at year '23' (Table 20).

Table 20 Demographic comparison between responders and non-responders at radiographical visit for year '23'

	YEAR '23'				
	X-ray Responders	X-ray Non-Responders	P value	Date skewness	Test used
Age (yrs) *n=328*	75.6	75.3	P=0.760 (>0.05)	Positive	Mann-Whitney U
Height (m) *n=331*	158.3	158.5	P=0.777 (>0.05)	Normal	Unpaired T-test
Weight (kg) *n=331*	69.6	68.3	P=0.158 (>0.05)	Positive	Mann-Whitney U
BMI (average) *n=331*	27.8	27.2	P=0.082 (>0.05)	Positive	Mann-Whitney U

5.5.3. Prevalence of osteoarthritis

Table 21 Distribution summary of participants with any presence of radiographic osteoarthritis at joint, foot and feet level (N=218)

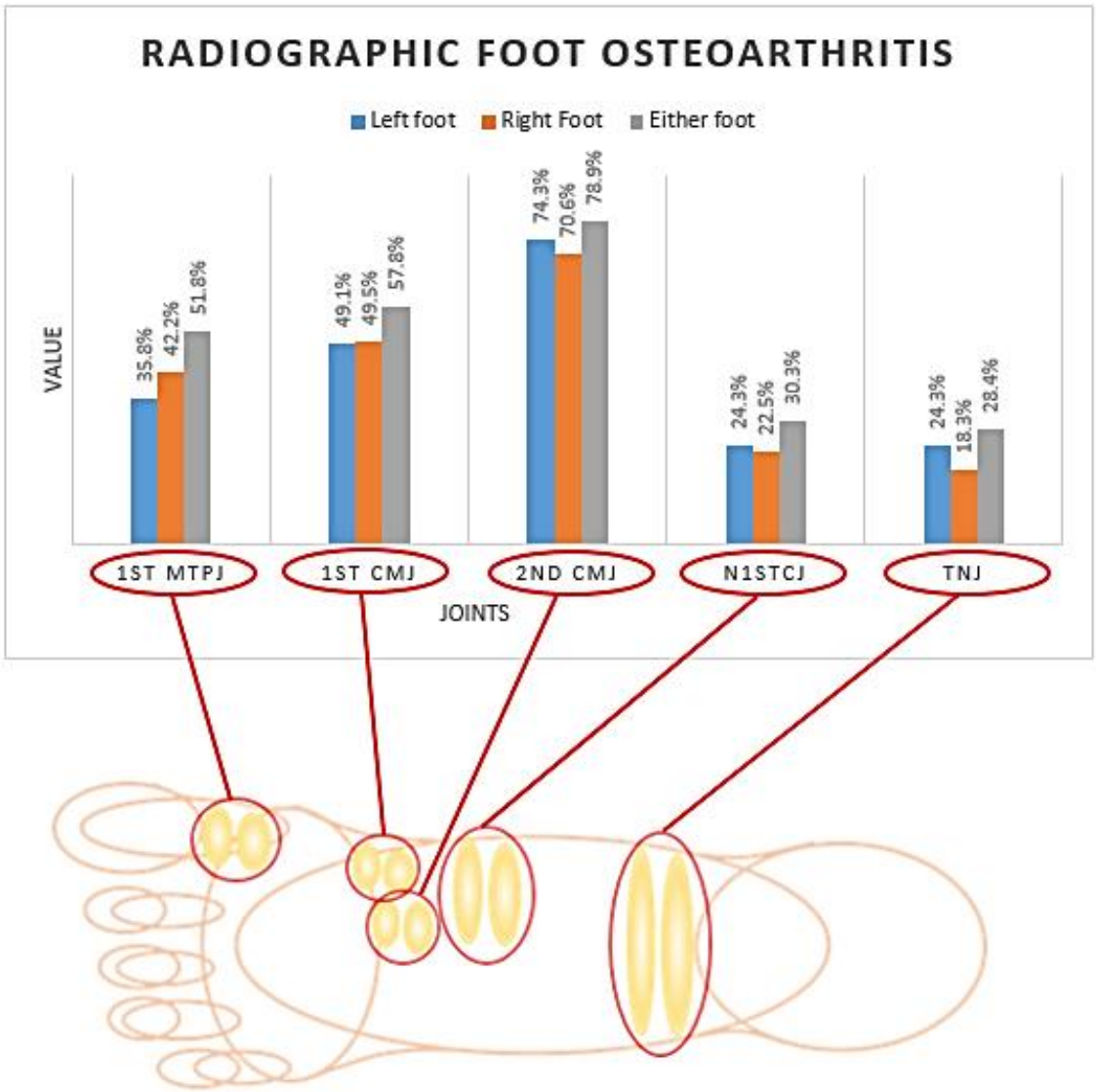
		Technique 1 prevalence: Conservative method		Technique 2 prevalence: Overscored method		Technique 3 prevalence: Ungradable excluded method	
Evaluation of OA		Left foot	Right foot	Left foot	Right foot	Left foot	Right foot
Single joint evaluated foot OA	**1st MTPJ**	35.8%	42.2%	42.7%	52.3%	31.2%	35.8%
	1st CMJ	49.1%	49.5%	65.1%	66.5%	45.9%	46.3%
	2nd CMJ	74.3%	70.6%	79.4%	74.8%	34.4%	29.8%
	N1stCJ	24.3%	22.5%	73.4%	74.8%	21.1%	20.2%
	TNJ	24.3%	18.3%	43.6%	39.9%	22.9%	17.9%
Polyarticular evaluated joint foot osteoarthritis (left and right foot specific)		88.1% (n=192)	87.6% (n=191)	95.0% (n=207)	96.3% (n=210)	77.1% (n=168)	78.0% (n=170)
Participants with any foot joint osteoarthritis (either left or right foot)*		**91.3% (n=199; N=218)**		**97.2% (n=212; N=218)**		**83.5% (n=182; N=218)**	

**LFA overall definition of foot OA/person-level foot OA.*

Table 21 summarises prevalence results of radiographic osteoarthritis in individual joints, foot and combined feet using different techniques as established in Chapter 4. Prevalence of radiographic osteoarthritis in the feet was 91.3% among older women from a UK cohort (199/218) using technique 1, which was identified as the chosen method for identifying radiographic osteoarthritis (Chapter 4). Graph 5 provides a summary of the prevalence findings established in Chapter 4 for radiographic osteoarthritis according to each joint and each foot.

At the individual joint level (Table 21), the highest prevalence of osteoarthritis in a joint was the 2nd CMJ joint and in decreasing order of prevalence, the 1st CMJ, 1st MTPJ, N1stCJ and the TNJ. The only difference in prevalence pattern of joints existing between the left, right and both feet is where the left foot demonstrated the same prevalence in both the Navicular 1st cuneiform joint and the Talonavicular joint.

Graph 1 Summary of radiographic osteoarthritis by foot in each joint



The forefoot joints (1st metatarsophalangeal, 1st cuneo-metatarsal joint and 2nd cuneo-metatarsal) were the joints with a higher prevalence in the right foot. The mid and rear foot joints (Navicular 1st cuneiform joint and talonavicular joint) demonstrated a higher prevalence in the left foot. Prevalence of radiographic foot osteoarthritis joint differences ranged between the left foot (50.0%), the right foot (52.3%) and both feet (50.5%) demonstrating a consistently large difference between the highest and lowest prevalence in the left, right and both feet (Graph 1). Ranking order of the prevalence of radiographic osteoarthritis according to each joint is presented in table 22.

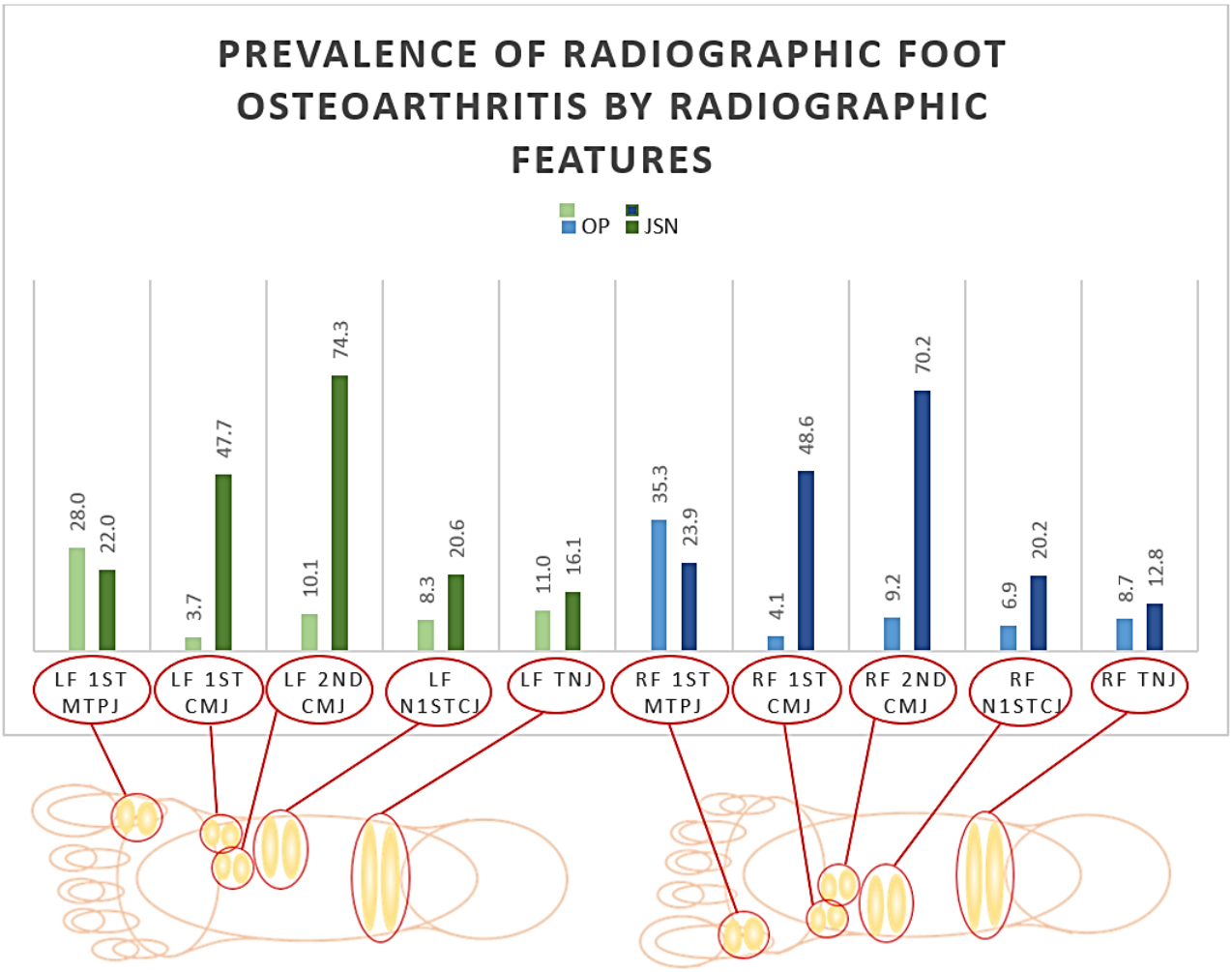
Table 22 Joint assessment ranking order

Sequence	Joint	Foot
1	1st metatarsophalangeal joint (1st MTPJ)	Left
2	1st metatarsophalangeal joint (1st MTPJ)	Right
3	1st cuneo-metatarsal joint (1st CMJ)	Left
4	1st cuneo-metatarsal joint (1st CMJ)	Right
5	2nd cuneo-metatarsal joint (2st CMJ)	Left
6	2nd cuneo-metatarsal joint (2st CMJ)	Right
7	Navicular 1st cuneiform joint (N1stCJ)	Left
8	Navicular 1st cuneiform joint (N1stCJ)	Right
9	Talonavicular Joint (TNJ)	Left
10	Talonavicular Joint (TNJ)	Right

5.5.3.1. Prevalence of radiographic osteoarthritis by osteophytic change and joint space narrowing and by individual joint

The prevalence of radiographic osteoarthritis by radiographic feature in each joint of both feet (established using technique 1 in Chapter 4) is summarised in Graph 2.

Graph 2 Prevalence of osteophytic change and joint space narrowing according to each joint



In all joints with the exception of the 1st metatarsophalangeal joints, features were shown to be higher in prevalence with joint space narrowing than with osteophytic change (Graph 2).

Table 23 Prevalence in rank order by radiographic feature

Joint	Left		Combined	Right	
	Osteophytic change	Joints space narrowing	OP & JSN	Osteophytic change	Joints space narrowing
1st MTPJ	1st	3rd	2nd	1st	3rd
1st CMJ	5th	2nd	3rd	5th	2nd
2nd CMJ	3rd	1st	1st	2nd	1st
N1stCJ	4th	4th	4th	4th	4th
TNJ	2nd	5th	5th	3rd	5th

**Order is ascending prevalence from 5th to 1st with 5th being the lowest prevalence and 1st being the highest*

The navicular 1st cuneiform joint was the only joint that consistently kept its relative position of prevalence alone and in combination of features whereby it remained the second lowest prevalence (4th in table 23) despite the difference between features being smaller in the talonavicular joint. This joint therefore shows the most consistently prevalent features in relative terms. Although the talonavicular joint was lowest in prevalence for joint space narrowing and combined features, a surprise was the osteophytic change which excluded the dorsoplantar projection (due to the design of the atlas) and yet was the 2nd and 3rd highest prevalence for this feature in the left and right foot respectively.

Additionally, the lowest prevalence values of osteophytic change were in the joints which demonstrated the second highest overall prevalence, the 2nd cuneo-metatarsal joints. The joints which demonstrated the smallest differences of 5.1% and 4.1% between the radiographic features were the left and right talonavicular joints respectively. Additional detailed analysis of radiographic osteoarthritis in the foot stratified according to severity of each joint is provided in appendix 11 and 12.

5.5.3.2. Prevalence of rOA stratified according to age and painful rOA according to age

Table 24 Radiographic foot joint osteoarthritis stratified according to age N=215

	Left foot n (%)						Right foot						Either foot (N=215)	Symptomatic radiographic osteoarthritis (N=188)
Age years (N=215)	**1st MTPJ**	**1st CMJ**	**2nd CMJ**	**N1stCJ**	**TNJ**	**Any joint**	**1st MTPJ**	**1st CMJ**	**2nd CMJ**	**N1stCJ**	**TNJ**	**Any joint**	**All joints**	**Any joint**
65-69 (20)	7 (35.0%)	11 (55.0%)	17 (85.0%)	2 (10.0%)	2 (10.0%)	18 (90.0%)	10 (50.0%)	9 (45.0%)	15 (75.0%)	1 (5.0%)	1 (5.0%)	18 (90.0%)	19 (95.0%)	6; 18 (33.3%)
70-74 (82)	32 (39.0%)	40 (48.8%)	58 (70.7%)	21 (25.6%)	19 (23.2)	75 (91.5%)	32 (39.0%)	42 (51.2%)	56 (68.3%)	16 (19.5%)	10 (12.2%)	74 (90.2%)	76 (92.7)	12; 75 (16.0%)
75-79 (58)	21 (36.2%)	33 (56.9%)	41 (70.7%)	9 (15.5%)	17 (29.3)	47 (81.0%)	28 (48.3%)	33 (56.9%)	42 (72.4%)	15 (25.9%)	14 (24.1%)	49 (84.5%)	48 (82.8)	12; 46 (26.1%)
80-84 (42)	12 (28.6%)	14 (33.3%)	33 (78.6%)	20 (47.6%)	12 (28.6%)	37 (88.1)	17 (40.5%)	14 (33.3%)	30 (71.4%)	16 (38.1%)	12 (28.6%)	36 (85.7%)	38 (90.5%)	9; 37 (24.3%)
85-89 (12)	5 (41.7%)	7 (58.3%)	9 (75.0%)	1 (8.3%)	2 (16.7%)	11 (91.7%)	4 (33.3%)	6 (50.0%)	8 (66.7%)	1 (8.3%)	2 (16.7%)	10 (83.3%)	11 (91.7%)	1; 11 (9.1%)
90-94 (1)	0 (0.0%)	0 (0.0%)	1 (100.0%)	0 (0.0%)	0 (0.0%)	1 (100.0%)	0 (0.0%)	1 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (100.0%)	1 (100.0%)	0; 1 (0.0%)

Age stratified prevalence of radiographic osteoarthritis (Table 24) in any joint in the left and right feet varied between 0% and 3.5%. On a person level, radiographic osteoarthritis in any joint of either foot was lowest among the 75 to 79 years age group. The highest prevalence was found to increase in groups after the age of 74. It is not surprising that the age group category of 91 to 94 represented small values across the different joints as this represented one person. Therefore, this group should be considered with this limitation and with the understanding that a higher number of participants would be required to make this category meaningful. In terms of individual results, the most remarkable result was the navicular 1st cuneiform joint where (excluding the 90-94 age group) this ranged between age groups of 39.3% in the left foot and 33.1% in the right foot. Symptomatic radiographic osteoarthritis demonstrated no obvious pattern in prevalence among the age groups which is consistent with the current body of evidence (Sharma et al. 2006).

5.5.3.3. Prevalence of foot rOA stratified according to Body Mass Index (BMI), and painful foot rOA with BMI

Table 25 Radiographic foot joint osteoarthritis stratified according to BMI N=217

		LEFT FOOT n (%)						RIGHT FOOT n (%)						EITHER FOOT n (%)	Symptomatic rOA (N=188)
BMI (N=217)	**Category**	**1st MTPJ**	**1st CMJ**	**2nd CMJ**	**N1stCJ**	**TNJ**	**Any joints**	**1st MTPJ**	**1st CMJ**	**2nd CMJ**	**N1stCJ**	**TNJ**	**Any joints**	**Any joints**	**Any joint**
< 18.5 (5)	**Underweight**	1 (20.0%)	2 (40.0%)	4 (80.0%)	1 (20.0%)	3 (60.0%)	4 (80.0%)	2 (40.0%)	2 (40.0%)	3 (60.0%)	1 (20.0%)	3 (60.0%)	3 (60.0%)	4 (80.0%)	1; 5 (20.0%)
18.5-24.99 (54)	**Normal**	16 (29.6%)	23 (42.6%)	41 (75.9%)	13 (24.1%)	13 (24.1%)	48 (88.9%)	16 (29.6%)	24 (44.4%)	37 (68.5%)	7 (13.0%)	10 (18.5%)	46 (85.2%)	49 (90.7%)	5; 46 (10.9%)
25.0-29.99 (99)	**Overweight**	38 (38.4%)	53 (53.5%)	75 (75.8%)	20 (20.2%)	19 (19.2%)	89 (89.9%)	44 (44.4%)	56 (56.6)	69 (69.7)	22 (22.2)	13 (13.1%)	90 (90.0%)	91 (91.9%)	17; 87 (19.5%)
30.0-34.99 (45)	**Obese – Class 1**	16 (35.6%)	22 (48.9%)	33 (73.3%)	13 (28.9)	10 (22.2%)	38 (84.4%)	22 (48.9%)	21 (46.7%)	36 (80.0%)	15 (33.3%)	10 (22.2%)	39 (86.7%)	39 (86.7%)	13; 39 (33.3%)
35.0-39.99 (12)	**Obese – Class 2**	5 (41.7%)	5 (41.7%)	6 (50.0%)	3 (25.0%)	7 (58.3)	10 (83.3%)	6 (50.0%)	3 (25.0%)	6 (50.0%)	2 (16.7%)	4 (33.3%)	10 (83.3%)	10 (83.3%)	4; 10 (40.0%)
40.0-49.99 (2)	**Obese – Class 3**	1 (50.0%)	1 (50.0%)	2 (100.0%)	2 (100.0%)	0 (0.0%)	2 (100.0%)	1 (50.0%)	1 (50.0%)	2 (100.0%)	1 (50.0%)	0 (0.0)	2 (100.0%)	2 (100.0%)	1; 1 (100.0%)

The prevalence of rOA, stratified according to BMI (Table 25), was varied between the left and right feet (0% to 2.3%). The person level radiographic osteoarthritis (presence of radiographic osteoarthritis in any joint of either foot) was found to be lowest in the underweight category and highest in the obese class 3 category. However, the obese class 3 category, like the highest age category, had a low number of participants (consisting of only two) and therefore should be interpreted with caution. The next highest prevalence among BMI group categories was the overweight category followed by the normal category and only at this point, the other categories of obese came into order. This is surprising as it would have been expected that increasing BMI would have shown correspondence directly with increasing radiographic foot osteoarthritis prevalence. The outlying categories (underweight and obese class 3) with the lowest number of participants created a greater difference in individual joint prevalence of radiographic foot osteoarthritis and therefore present the need for further investigation. As there was no significant difference between responders and non-responders (Table 20), this cannot be attributed as a bias arising from the participants not being representative of the general population. When excluding these outlying categories, the talonavicular joint demonstrated the greatest difference between categories with 39.1% in the left foot and 20.2% on the right foot. Participants with co-existing radiographic foot osteoarthritis and foot pain demonstrated increasing prevalence with increasing BMI from normal to obese class 3 BMI categories but notably underweight participants were a similar prevalence to overweight participants.

5.6. Prevalence of foot pain

Of the sample (n=334), participants who did not fully complete the self-assessed pain questionnaires and those who did not return the questionnaires accounted for 19 participants. Of the remaining participants in this sample (n=315), prevalence of foot pain which was experienced at any point in a participant's life for one day or longer was established (Table 26) as 30.5% in a UK population-based cohort of older women (96/315). Prevalence of foot pain which was experienced in the past month for one day or longer was established as 20.0% of participants (63/315).

5.6.1. Generalised Foot Pain - <u>ever</u> experienced foot pain lasting one day or longer (MFPDI Foot manikin)

Table 26 Prevalence of having ever experienced foot pain lasting one day or longer (N=315)

Aspect or region	No.	Structure	Left % (315)	Right % (315)
Dorsal	1	1st digit	4.8% (15)	6.0% (19)
	2	2nd digit	3.2% (10)	3.5% (11)
	3	3rd digit	2.9% (9)	2.2% (7)
	4	4th digit	3.2% (10)	3.2% (10)
	5	5th digit	1.3% (4)	1.9% (6)
	1-5	1st – 5th digits	7.0% (22)	7.9% (25)
	6	1st metatarsal	8.6% (27)	6.3 (20)
	7	2nd metatarsal	1.9% (6)	1.9% (6)
	8	3rd metatarsal	1.3% (4)	1.0% (3)
	9	4th metatarsal	1.0% (3)	1.6% (5)
	10	5th metatarsal	1.6% (5)	1.0% (3)
	6-10	6th – 10th metatarsals	10.8% (34)	7.6% (24)
	11	Midfoot	4.1% (13)	4.1% (13)
	12	Ankle	3.2% (10)	4.4% (14)
	1-12	All structures	17.5% (55)	18.1% (57)
Plantar	13	1st digit	3.2% (10)	2.9% (9)
	14	2nd digit	1.6% (5)	1.3% (4)
	15	3rd digit	1.3% (4)	1.3% (4)
	16	4th digit	1.6% (5)	1.6% (5)
	17	5th digit	1.0% (3)	1.6% (5)
	13-17	1st – 5th digits	4.1% (13)	3.8% (12)
	18	1st metatarsal	4.4% (14)	3.8% (12)
	19	2nd metatarsal	5.1% (16)	3.8% (12)
	20	3rd metatarsal	4.8% (15)	3.5% (11)
	21	4th metatarsal	2.2% (7)	1.6% (5)
	22	5th metatarsal	1.3% (4)	2.2% (7)
	18-22	1st – 5th metatarsals	9.2% (29)	7.9% (25)
	23	Arch	2.9% (9)	3.5% (11)
	24	Midfoot	3.8% (12)	4.4% (14)
	25	Heel	5.1% (16)	5.4% (17)
	13-25	Any structure	17.8% (56)	16.5% (52)
Dorsal & plantar	1-25	Any structure	24.4% (77)	24.4% (77)
			30.5% (96)	

5.6.2. Generalised Foot Pain – Foot pain in the past month lasting one day or longer (MFPDI Foot manikin)

Table 27 Prevalence of having experienced foot pain in the past month lasting one day or longer (N=315)

Aspect or region	No.	Structure	Left % (315)	Right % (315)
Dorsal	1	1st digit	4.4% (14)	5.7% (18)
	2	2nd digit	1.6% (5)	2.9% (9)
	3	3rd digit	1.6% (5)	1.9% (6)
	4	4th digit	1.9% (6)	2.5% (8)
	5	5th digit	0.6% (2)	1.6% (5)
	1-5	1st – 5th digits	5.7% (18)	6.9% (22)
	6	1st metatarsal	5.7% (18)	3.5% (11)
	7	2nd metatarsal	1.3% (4)	0.6% (2)
	8	3rd metatarsal	1.0% (3)	0.3% (1)
	9	4th metatarsal	1.0% (3)	0.6% (2)
	10	5th metatarsal	0.6% (2)	0.3% (1)
	6-10	1st – 5th metatarsals	6.7% (21)	4.1% (13)
	11	Midfoot	4.2% (13)	3.8% (12)
	12	Ankle	2.9% (9)	4.2% (13)
	1-12	All structures	12.7% (40)	12.1% (38)
Plantar	13	1st digit	4.2% (13)	3.2% (10)
	14	2nd digit	1.9% (6)	1.3% (4)
	15	3rd digit	1.6% (5)	1.3% (4)
	16	4th digit	1.9% (6)	1.3% (4)
	17	5th digit	1.3% (4)	1.0% (3)
	13-17	1st – 5th digits	4.4% (14)	3.5% (11)
	18	1st metatarsal	3.2% (10)	3.2% (10)
	19	2nd metatarsal	3.8% (12)	2.9% (9)
	20	3rd metatarsal	3.5% (11)	3.2% (10)
	21	4th metatarsal	1.6% (5)	1.9% (6)
	22	5th metatarsal	1.0% (3)	0.6% (2)
	18-22	1st – 5th metatarsals	6.7% (21)	5.7% (18)
	23	Arch	1.9% (6)	2.2% (7)
	24	Midfoot	2.5% (8)	3.2% (10)
	25	Heel	3.2% (10)	2.9% (9)
	13-25	Any structure	13.7% (43)	12.1% (38)
Dorsal & plantar	1-25	Any structure	18.7% (59)	15.6% (49)
			20.0% (63)	

Table 27 shows that the combined metatarsals of both feet had a higher prevalence of pain in the left foot than right, in both dorsal and plantar surfaces. This was the same for plantar surface combined digits where the left foot had higher prevalence of pain marked by participants as compared with the right foot. However, at the dorsal surface, the right foot had higher prevalence of pain than the left foot. Joints which were not combined with

others such as the midfoot, ankle and heel had differences between left and right foot pain ranging from 0.3% to 1.3%.

Table 28 Cross tabulation of participants foot pain experience in the past month or ever

		Ever experienced foot pain ≥ 1 day	
		No	**Yes**
Experienced foot pain in the last month ≥ 1 day	**No**	0.0% (0)	35.4% (35)
	Yes	0.0% (0)	64.6% (64)
	Totals	0.0% (0)	100% (99)

Further to the closed questions asked in relation to having had foot pain ever in their lifetime and in the past month, a cross-tabulation (Table 28) demonstrated that no participants answered the question inappropriately by stating they had foot pain in the last month but hadn't ever had it in their lifetime.

Of 99 participants who experienced one day or more of foot pain in the course of their life, 64.6% experienced foot pain in the past month. The proportion of participants who had experienced foot pain was high, however it corresponded well to the cross tabulated pain in the last month and having had an experience ever whereby no participants stated they had foot pain in the last month if they hadn't documented having experienced pain ever in their life. This demonstrated that the question was appropriately asked and answered in the questionnaire.

5.6.3. Global Foot Pain

Table 29 Manchester Foot Pain and Disability Index 17 (MFPDI) response frequencies of Australian populations and a UK population-based cohort of women (NWAHS (W) N=135; NWASHS (Yrs) N=57; C1000W N=118)

Question: ***'Because of pain in my feet…'***	**None of the time (n)**	**On some days (n)**	**On most days (n)**
I avoid walking outside at all	89.8% (106)	8.5% (10)	1.7% (2)
I avoid walking long distances	44.1% (52)	43.2% (51)	12.7% (15)
I don't walk in a normal way	66.9% (79)	20.3% (24)	12.7% (15)
I walk slowly	41.5% (49)	39.0% (46)	19.5% (23)
I have to stop and rest my feet	73.7% (87)	18.6% (22)	7.6% (9)
I avoid hard or rough surfaces when possible	40.7% (48)	40.7% (48)	18.6% (22)
I avoid standing for a long time	32.2% (38)	41.5% (49)	26.3% (31)
I catch the bus or use the car more often	30.5% (36)	37.3% (44)	32.2% (38)
I need help with housework/shopping	75.4% (89)	13.6% (16)	11.0% (13)
I get irritable when my feet hurt	66.9% (79)	29.7% (35)	3.4% (4)
I feel self-conscious about my feet	74.6% (88)	15.3% (18)	10.2% (12)
I feel self-conscious about the shoes I have to wear	71.2% (84)	20.3% (24)	8.5% (10)
I still do everything but with more pain and discomfort	43.2% (51)	40.7% (48)	16.1% (19)
I have constant pain in my feet	57.6% (68)	29.7% (35)	12.7% (15)
My feet are worse in the morning	71.2% (84)	21.2% (25)	7.6% (9)
My feet are more painful in the evening	63.6% (75)	27.1% (32)	9.3% (11)
I get shooting pains in my feet	72.0% (85)	22.9% (27)	5.1% (6)

**Participants were all women who had answered positively to having pain 'most days' in the last month (NWAHS N=135; C1000W N=118)*

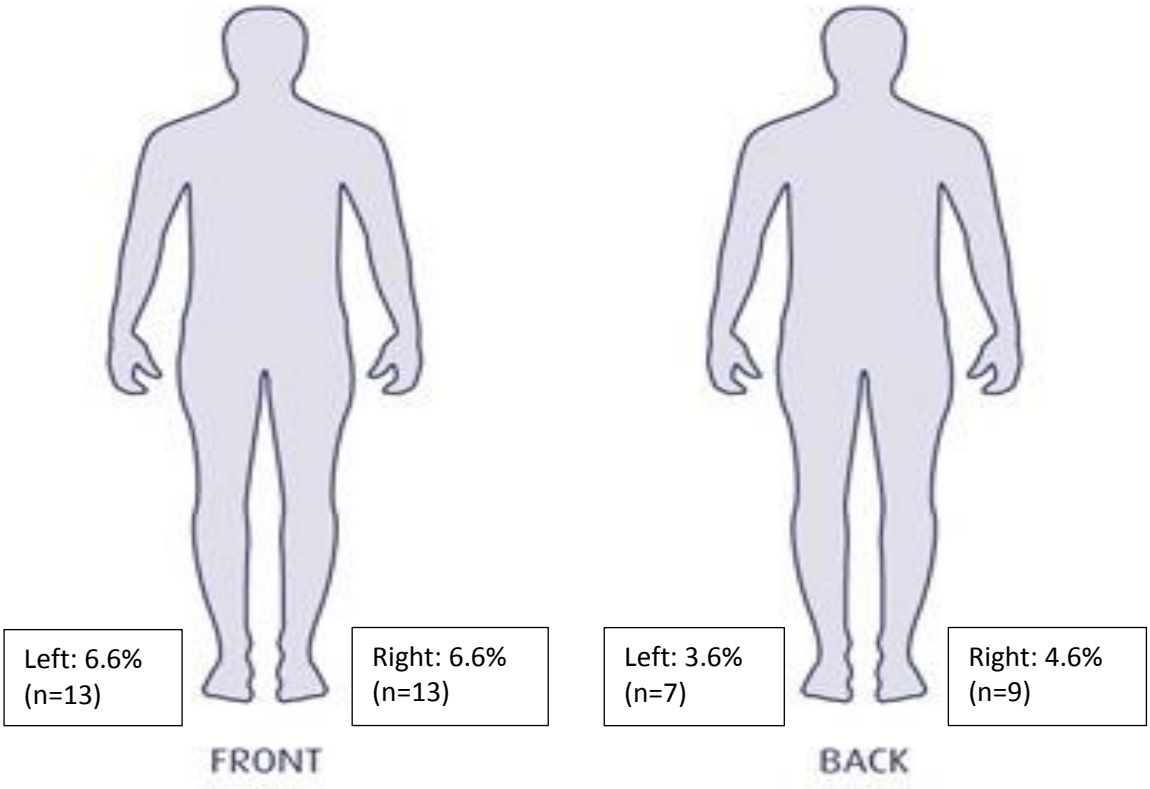
[¥]Participants were stratified according to gender. Data for women are presented in the table

[‡]Participants were stratified according to ag. Data for participants aged 71 to 90 years are presented in the table.

Overall pain prevalence according to the Manchester Foot Pain and Disability Index (MFPDI-17) was 51.7% (n=116). This was calculated by the selection of at least one item as being 'on some days' or 'on most days'.

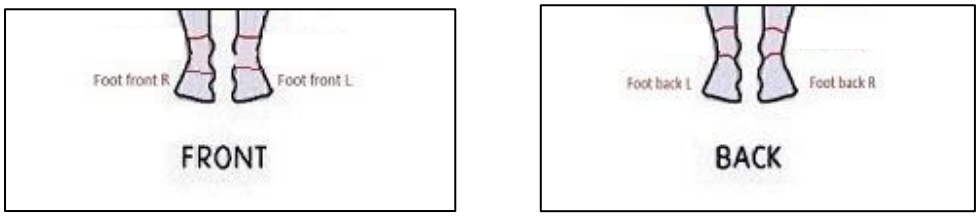
5.5.4 Global Foot Pain: Full body, shaded foot diagram

Figure 17 Global foot pain: Self-reported foot pain on most days in the last three months (marked with shading) N=197*



**Four versions of the questionnaire existed. Version 2 (N=118) used a footless diagram which was excluded but versions 1, 3 and 4 used the same diagram as shown above.*

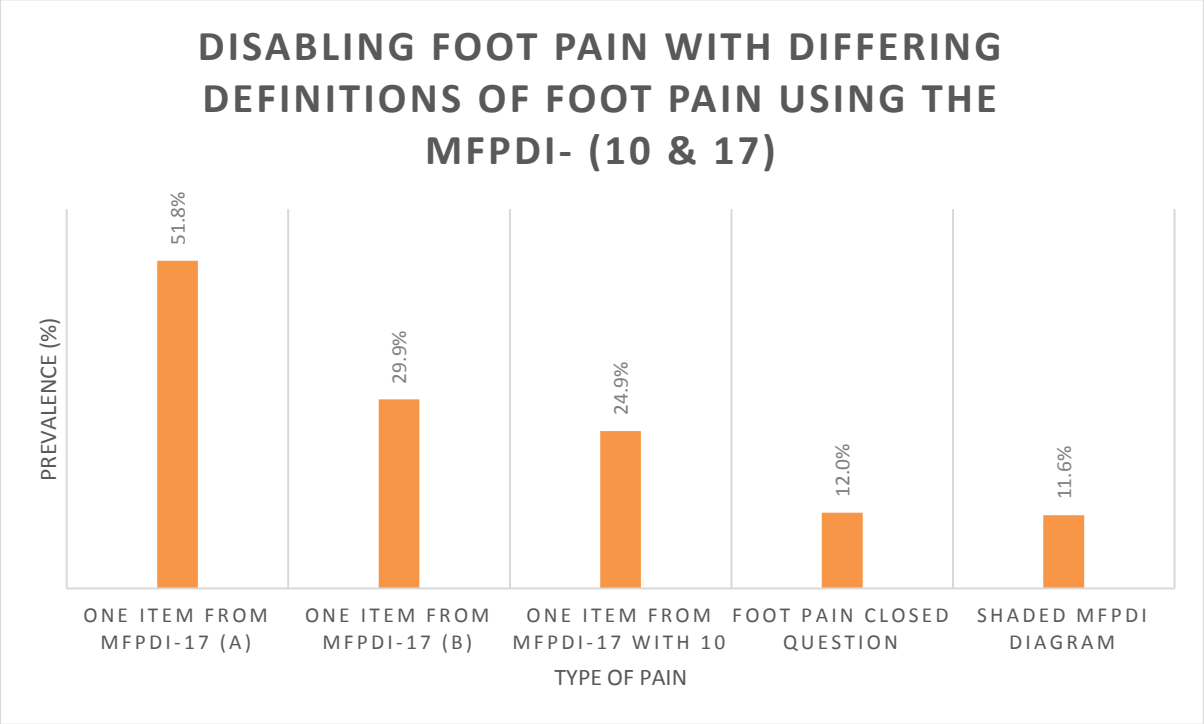
Template diagrams showing foot pain classifications



Global foot pain was found to be low in both feet from the anterior (front) and posterior (back) aspects. Foot pain in the feet (combined left and right views) was found to be 5.7% (n=18; N=315) with ankle pain found to be 4.4% (n=14; N=315) with the further combination of ankle and foot pain providing a prevalence of 7.6% (n=24; N=315). Global foot pain prevalence is thus considerably lower than that established in patient reported foot specific shaded foot pain manikins and single foot pain questioning, with the exception of clinician diagnosed foot pain (MFPDI manikin diagrams and single closed questioning of foot pain).

5.6.3.1. Global Foot Pain using Disabling foot pain measures

Graph 3 Differing definitions to establish disabling foot pain



1. **One item from MFPDI-17 (A):** Manchester Foot Pain and Disability Index (17) among the UK population-based cohort of older women demonstrated foot pain prevalence as **51.8%** (N=224; n=116).
2. **One item from MFPDI-17 (B):** Manchester Foot Pain and Disability Index (17) among the UK population-based cohort of older women demonstrated foot pain prevalence as **29.9%** (N=224; n=67).
3. **One item from MFPDI-17 with 10:** The grouping using at least one item of the MFPDI-10 'On most/every day(s)' with one positive item from the MFPDI-17, established a prevalence of **24.9%** (n=55; N=224).
4. **Foot pain closed question:** The grouping of at least one item of foot pain in the MFPDI-10 'On most/every day(s)' with the closed question provided a prevalence of **12.0%** (n=28; N=233).
5. **Shaded MFPDI diagram:** The combination of one item of the MFPDI-10 'On most/every day(s)' and one area of the shaded manikin gave a prevalence of **11.6%** (n=27; N=233).

5.6.3.2. Prevalence of Global Foot Pain stratified according to age

Table 30 Global Foot Pain (shaded MFPDI foot pain manikin) stratified according to age N=312

	N=312	LEFT FOOT n (%)						RIGHT FOOT n (%)						EITHER FOOT N (%)	EITHER FOOT & VIEWS n (%)
Aspect	**Age Years (N)**	**Digits**	**Metatarsals**	**Midfoot**	**Ankle**		**Any area**	**Digits**	**Metatarsals**	**Midfoot**	**Ankle**		**Any area**	**Any area**	**Any area**
Dorsal	65-69 (31)	2 (6.5%)	3 (9.7%)	1 (3.2%)	0 (0.0%)		5 (16.1%)	4 (12.9%)	1 (3.2%)	0 (0.0%)	0 (0.0%)		5 (16.1%)	7 (22.6%)	9 (29.0%)
	70-74 (124)	5 (4.0%)	7 (5.6%)	6 (4.8%)	4 (3.2%)		11 (8.9%)	5 (4.0%)	4 (3.2%)	4 (3.2%)	5 (4.0%)		8 (6.5%)	16 (12.9%)	17 (13.7%)
	75-79 (87)	5 (5.7%)	8 (9.2%)	3 (3.4%)	3 (3.4%)		12 (13.8%)	6 (6.9%)	6 (6.9%)	5 (5.7%)	4 (4.6%)		12 (13.8%)	17 (19.5%)	19 (21.8%)
	80-84 (50)	6 (12.0%)	3 (6.0%)	3 (6.0%)	2 (4.0%)		10 (20.0%)	6 (12.0%)	2 (4.0%)	3 (6.0%)	3 (6.0%)		11 (22.0%)	13 (26.0%)	16 (32%)
	85-89 (19)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.3%)		2 (10.5%)	1 (5.3%)	0 (0.0%)	0 (0.0%)	2 (10.5%)		2 (10.5%)	2 (10.5%)	2 (10.5%)
	90-94 (1)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		0 (0.0%)	0 (0.0%)	0 (0%)
Plantar	**Age Years (N)**	**Digits**	**Metatarsals**	**Arch**	**Midfoot**	**Heels**	**Any area**	**Digits**	**Metatarsals**	**Arch**	**Midfoot**	**Heels**	**Any area**	**Any area**	
	65-69 (31)	2 (6.5%)	4 (12.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	5 (16.1%)	2 (6.5%)	4 (12.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	6 (19.4%)	8 (25.8%)	
	70-74 (124)	3 (2.4%)	3 (2.4%)	5 (4.0%)	5 (4.0%)	10 (8.1%)	12 (9.7%)	3 (2.4%)	4 (3.2%)	4 (3.2%)	7 (5.6%)	10 (8.1%)	10 (8.1%)	13 (10.5%)	
	75-79 (87)	4 (4.6%)	10 (11.5%)	1 (1.1%)	4 (4.6%)	3 (3.4%)	14 (16.1%)	2 (2.3%)	6 (6.9%)	2 (2.3%)	2 (2.3%)	4 (4.6%)	10 (11.5%)	13 (14.9%)	
	80-84 (50)	5 (10.0%)	4 (8.0%)	3 (6.0%)	2 (4.0%)	2 (4.0%)	11 (22.0%)	4 (8.0%)	4 (8.0%)	4 (8.0%)	3 (6.0%)	2 (4.0%)	11 (22.0%)	13 (26.0%)	
	85-89 (19)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.3%)	1 (5.3%)	1 (5.3%)	0 (0.0%)	0 (0.0%)	1 (5.3%)	1 (5.3%)	1 (5.3%)	1 (5.3%)	2 (10.5%)	
	90-94 (1)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	

Foot pain of either surface (dorsoplantar or dorsal) of either the left or right foot demonstrated no real pattern and was more varied and sporadic when stratified according to age (Table 30). Of minor relevance was the decrease of foot pain prevalence in three categories in order of increasing age after the age of 80 until the age of 94 (80-84, 85-89 and 90-94). However, the last category consisted of one participant and, unlike the other stratified data, was an outlying category where more participants would be required to provide meaningful interpretation. This varied pattern of prevalence across age group categories is evident in both left and right feet and in both views. As only two relevant categories demonstrated a possible pattern, it is best to conclude that the results were spurious, showing no true pattern of foot pain prevalence.

5.6.3.3. Prevalence of Global Foot Pain stratified according to BMI

Table 31 Global foot pain (shaded MFPDI foot pain manikin) stratified according to BMI (N=313)

	N=313	LEFT FOOT n (%)						RIGHT FOOT n (%)						EITHER FOOT N (%)	EITHER FOOT & VIEWS n (%)
Aspect	**BMI (N)**	**Digits**	**Mets.**	**Midfoot**	**Ankle**		**Any area**	**Digits**	**Mets.**	**Midfoot**	**Ankle**		**Any area**	**Any Area**	**Any area**
Dorsal	Underweight < 18.5 (5)	1 (20.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (20.0%)	0 (0.0%)	1 (20.0%)	0 (0.0%)	0 (0.0%)		1 (20.0%)	1 (20.0%)	1 (20.0%)
	Normal – 18.5-24.99 (88)	3 (3.4%)	1 (1.1%)	2 (2.3%)	3 (3.4%)		5 (5.7%)	2 (2.3%)	0 (0.0%)	1 (1.1%)	4 (4.5%)		4 (4.5%)	6 (6.8%)	7 (8.0%)
	Overweight – 25.0-29.99 (140)	6 (4.3%)	12 (8.6%)	4 (2.9%)	4 (2.9%)		18 (12.9%)	8 (5.7%)	7 (5.0%)	5 (3.6%)	7 (5.0%)		17 (12.1%)	26 (18.6%)	30 (21.4%)
	Obese – class 1 – 30.0-34.99 (58)	6 (10.3%)	5 (8.6%)	5 (8.6%)	1 (1.7%)		11 (19.0%)	9 (15.5%)	4 (6.9%)	5 (8.6%)	1 (1.7%)		12 (20.7%)	15 (25.9%)	18 (31.0%)
	Obese – class 2 – 35.0-39.99 (20)	1 (5.0%)	3 (15.0%)	2 (10.0%)	1 (5.0%)		4 (20.0%)	2 (10.0%)	1 (5.0%)	2 (10.0%)	1 (5.0%)		3 (15.0%)	6 (30.0%)	6 (30.0%)
	Obese – class 3 – 40.0-49.99 (2)	1 (50.0%)	0 (0.0%)	0 (0.0%)	1 (50.0%)		1 (50.0%)	1 (50.0%)	0 (0.0%)	0 (0.0%)	1 (50.0%)		1 (50.0%)	1 (50.0%)	1 (50.0%)
Plantar	BMI (N)	**Digits**	**Mets.**	**Arch**	**Midfoot**	**Heel**	**Any area**	**Digits**	**Mets.**	**Arch**	**Midfoot**	**Heel**	**Any area**	**Any area**	
	Underweight < 18.5 (5)	1 (20.0%)	1 (20.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)	1 (20.0%)	1 (20.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)	1 (20.0%)	
	Normal – 18.5-24.99 (88)	2 (2.3%)	1 (1.1%)	0 (0.0%)	1 (1.1%)	3 (3.4%)	5 (5.7%)	3 (3.4%)	1 (1.1%)	4 (4.5%)	3 (3.4%)	1 (1.1%)	6 (6.8%)	6 (6.8%)	
	Overweight – 25.0-29.99 (140)	5 (3.6%)	13 (9.3%)	3 (2.1%)	6 (4.3%)	6 (4.3%)	21 (15.0%)	3 (2.1%)	11 (7.9%)	3 (2.1%)	5 (3.6%)	6 (4.3%)	16 (11.4%)	21 (15.0%)	
	Obese – class 1 – 30.0-34.99 (58)	5 (8.6%)	5 (8.6%)	2 (3.4%)	2 (3.4%)	6 (10.3%)	12 (20.7%)	3 (5.2%)	4 (6.9%)	2 (3.4%)	3 (5.2%)	8 (13.8%)	12 (20.7%)	16 (27.6%)	
	Obese – class 2 – 35.0-39.99 (20)	0 (0.0%)	1 (5.0%)	3 (15.0%)	2 (10.0%)	1 (5.0%)	3 (15.0%)	0 (0.0%)	1 (5.0%)	1 (5.0%)	2 (10.0%)	1 (5.0%)	2 (10.0%)	4 (20.0%)	

	Obese – class 3 – 40.0-49.99 (2)	1 (50.0%)	0 (0.0%)	1 (50.0%)	1 (50.0%)	0 (0.0%)	1 (50.0%)	1 (50.0%)	0 (0.0%)	1 (50.0%)	1 (50.0%)	1 (50.0%)	1 (50.0%)	1 (50.0%)

A general pattern emerged among the categories after the underweight category, whereby increasing BMI demonstrated increasing foot pain (in any joint of either foot) with the exception of the obese class 2 category (Table 31). Importantly, the normal category demonstrated the lowest prevalence of foot pain of all categories, 12% lower than the next most prevalent category of underweight. The obese 3 category had a small number of participants (n=2) and was therefore an outlying category which would have required more participants to be able to demonstrate a meaningful contribution to the discussion. Plantar aspect foot pain demonstrated the same pattern as foot pain in either view (plantar or dorsoplantar) in any joint in the left foot and the right foot and also either feet. However, dorsal foot pain demonstrated a more consistent pattern of increasing foot pain with increasing BMI from the 'Normal' category of BMI which was consistent with both left and right feet.

5.6.4 Foot Joint Pain: Clinician diagnosed foot pain

Table 32 Current foot joint pain diagnosed by passive joint motion by a clinician

Joint (Left N; Right N)	Left	Right
1st MTPJ (203; 201)	2.0% (4)	1.5% (3)
2nd MTPJ (203; 203)	0.0% (0)	0.0% (0)
3rd MTPJ (203; 203)	0.0% (0)	0.0% (0)
4th MTPJ (203; 203)	0.0% (0)	0.0% (0)
5th MTPJ (203; 203)	0.0% (0)	0.0% (0)
1st CMJ (202; 203)	0.0% (0)	0.0% (0)
2nd CMJ (202; 203)	0.5% (1)	0.0% (0)
N1stCJ (202; 202)	0.0% (0)	0.0% (0)
Midfoot (202; 203)	0.0% (0)	0.0% (0)
Subtalar (202; 203)	0.5% (1)	0.5% (1)
Total (202; 201)	1.5% (6)	1.0% (4)

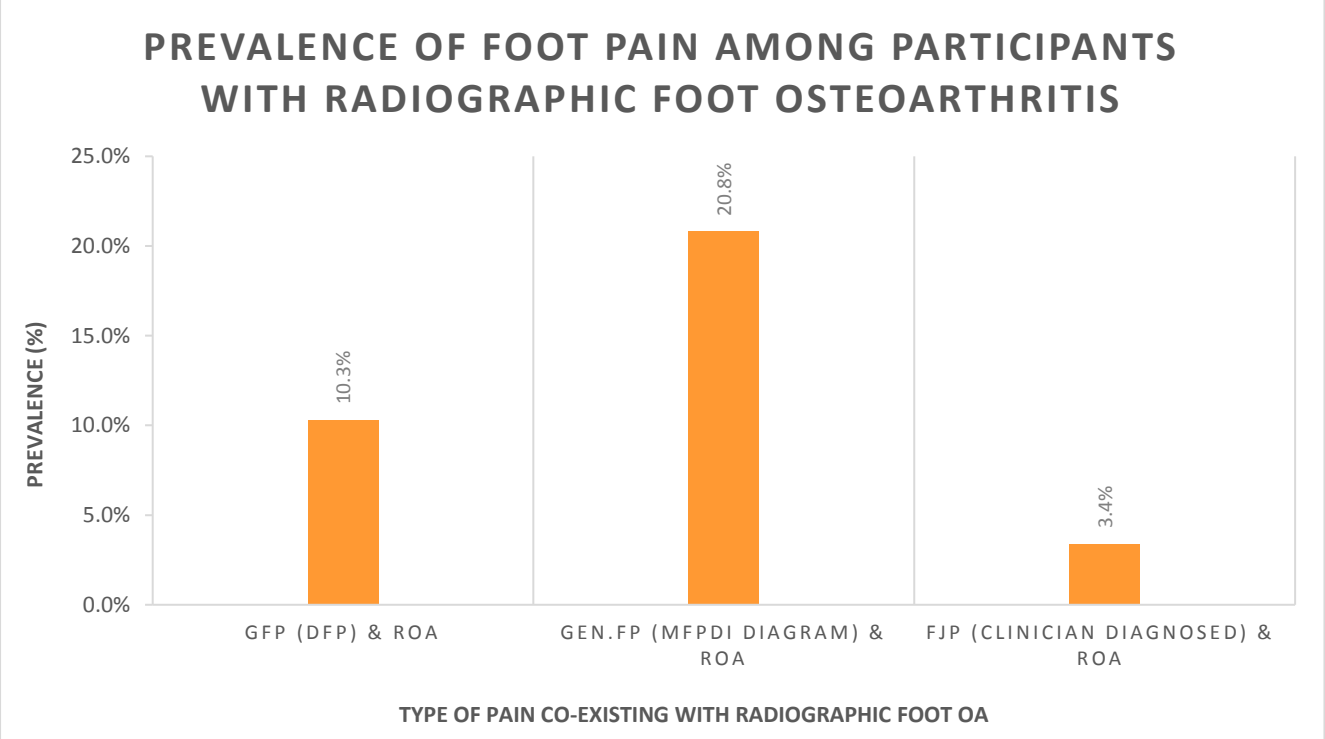
*The same denominator was not used for the dataset as this would have prevented capture of the few participants who did exhibit foot joint pain in the respective joints.

Overall prevalence of clinician diagnosed foot pain (where both feet were combined) was found to be **3.0%** (n=6; N=200).

5.7. Presence of radiographic foot osteoarthritis and co-existing pain

Of those from the sample who returned and fully completed their questionnaires (n=210), 20.8% of older female participants from the UK population-based cohort of older women (40/192) had foot pain (according to the case definition of global foot pain) which co-existed with radiographic foot osteoarthritis. Of individuals with radiographic foot osteoarthritis, 79.2% reported no foot pain (152/192) (Graph 4).

Graph 4 Prevalence of foot pain and co-existing radiographic foot osteoarthritis



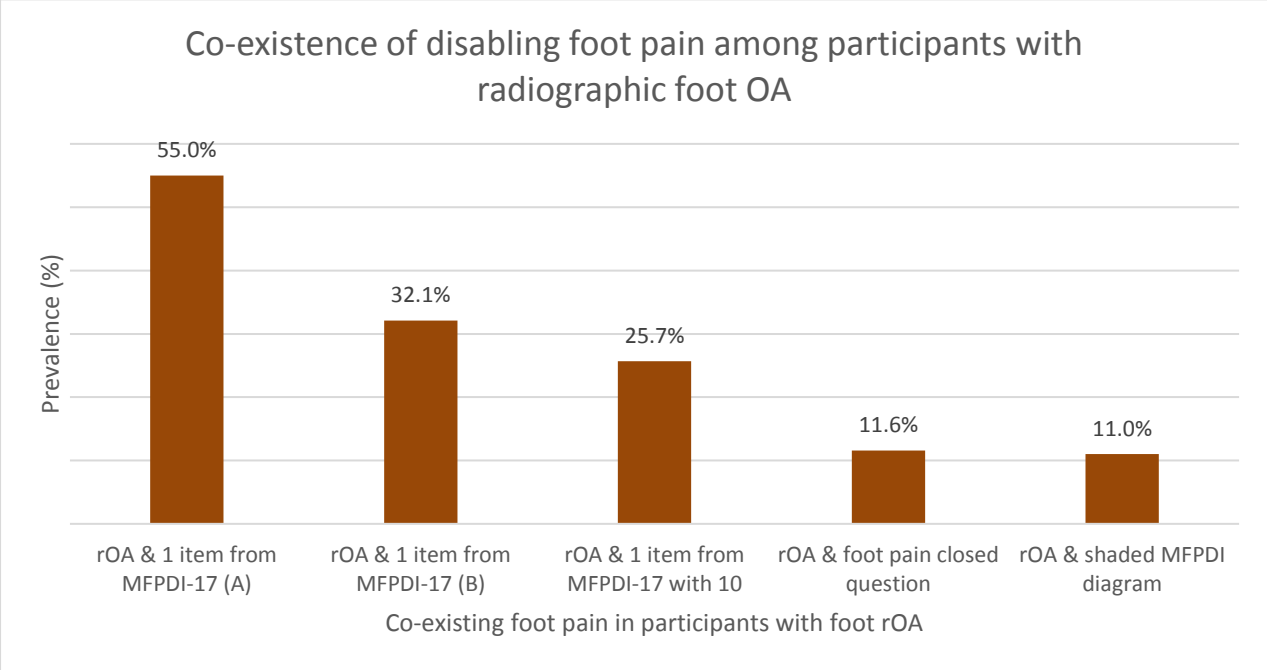
Global Foot Pain, demonstrated using disabling foot pain as established through participants identifying foot pain 'most days' for at least one item of the ten used in the definition described in section 5.6.3.1. was found to co-exist with radiographic foot osteoarthritis in 10.3% (n=16; N=155) of participants.

Generalised Foot Pain, demonstrated using co-existing radiographic foot osteoarthritis and foot pain identified as one item from the Manchester Foot Pain and Disability Index (MFPDI shaded diagram), was found in 20.8% of participants (n=40; N=192).

Foot Joint Pain was demonstrated using clinician diagnosed foot pain, and co-existing radiographic osteoarthritis was found to be present in 3.4% (n=4; N=119) of participants.

5.7.1. Additional co-existing Global Foot Pain: Disabling foot pain

Graph 5 Differing definitions to establish disabling foot pain



1. **Radiographic osteoarthritis with one item from MFPDI-17 (A):** Manchester Foot Pain and Disability Index (17) among the UK population-based cohort of older women demonstrated foot pain prevalence as **55.0%** (n=77; N=140).
2. **Radiographic osteoarthritis with one item from MFPDI-17 (B):** Manchester Foot Pain and Disability Index (17) among the UK population-based cohort of older women demonstrated foot pain prevalence as **32.1%** (n=45; N=140).
3. **Radiographic osteoarthritis with one item from MFPDI-17 with 10:** the grouping responding positively to at least one item of the MFPDI-10 'on most/every day(s)' with one positive item from the MFPDI-17, established a prevalence of **25.7%** (n=36; N=140).
4. **Radiographic osteoarthritis with foot pain closed question:** the grouping responding positively to at least one item of foot pain in the MFPDI-10 'on most/every day(s)' with the closed question provided a prevalence of **11.6%** (n=17; N=146).
5. **Radiographic osteoarthritis with shaded MFPDI diagram:** The combination of one item of the MFPDI-10 'on most/every day(s)' and one area of the shaded manikin gave a prevalence of **11.0%** (n=16; N=146).

5.8. Summary of results

5.8.1. Description of the prevalence of radiographic foot osteoarthritis

In a large cross-section of women from a UK population-based cohort of older women, prevalence was found to be high (91.3%). Joints were ranked in terms of prevalence from highest to lowest; 2nd CMJ, 1st CMJ, 1st MTPJ, N1stCJ and TNJ. The TNJ, although lowest, was representative of only one radiographic projection. When stratified according to age, the highest prevalence was among older age groups, and according to BMI no recognisable pattern could be identified.

5.8.2. Description of the prevalence of foot pain

Self-reported foot pain prevalence in the past month among participants was (20.0%). Foot pain demonstrated a large degree of variability depending on the definition used. Generalised Foot Pain defined using self-reported foot manikins was higher than Global Foot Pain where participants shaded their pain on full body manikins and foot data were extracted. Foot joint pain identified by a clinician diagnosis was found to be very low. Finally, when stratified according to age, foot pain demonstrated no obvious pattern, but when stratified according to BMI, there was increasing prevalence of foot pain with increasing BMI.

5.8.3. Analysis of the relationship between radiographic foot osteoarthritis and foot pain

Painful (Gen.FP) osteoarthritis was shown to exist in around 20.8% participants. Global Foot Pain co-existing with radiographic foot osteoarthritis was found to be prevalent in 10.3% of participants, half the number as compared with Generalised Foot Pain, with co-existing foot joint pain diagnosed by a clinician considerably lower. Global Foot Pain using disabling foot pain measures were found to be similar to standalone disabling foot pain results and differences were minimal between study groups. When stratified, age had little relevance to any identifiable pattern, however, BMI demonstrated increasing painful radiographic foot osteoarthritis with increasing BMI groups.

5.9. Discussion

To the knowledge of the author this is the first study to have investigated asymptomatic and symptomatic radiographic foot osteoarthritis in a large sample of older women. Prevalence of overall radiographic foot osteoarthritis was found to be comparably high at 91.3% for those aged 69 to 91 and the self-reported lifetime experience of foot pain among women aged 60 to 91 was 30.5%. By joint, radiographic osteoarthritis was found to exist in ranked order as the following; 2nd CMJ (78.9%), 1st CMJ (57.8%), 1st MTPJ (51.8%), N1stCJ (30.3%) and TNJ (28.4%). Of note, co-existing radiographic foot osteoarthritis and Global Foot Pain identified by self-reported foot pain was 20.8% (marginally higher than foot pain irrespective of radiographic foot osteoarthritis at 20.5%). Clinician

diagnosed foot joint pain specific to individual joint radiographic foot osteoarthritis was found to be 3.4%. This study confirms the complex problem that exists in defining symptomatic radiographic foot osteoarthritis.

5.9.1 Prevalence of radiographic foot osteoarthritis

The prevalence of radiographic foot osteoarthritis in this study is similar to that reported in an Australian population (93%) (Menz et al. 2009) with the exception of the first cuneo-metatarsal joint in both feet. Although Menz et al. (2009) included men in their research, whereby a lower prevalence would have been expected compared to the female only Chingford 1000 Women study, these small differences may be explainable through other cohort characteristics such as the cultural and physiological differences. However, this would require further research to compare the Chingford women with a cohort of men with similar characteristics. The difference is sufficiently small and the methods are similar whereby the results of the Chingford women can be considered valid in the context of the body of research that currently exists.

The most prevalent joint was the 2nd cuneo-metatarsal joint and in decreasing order of prevalence, the 1st cuneo-metatarsal joint, 1st metatarsophalangeal joint, navicular 1st cuneiform joint and the talonavicular joint. This forms an important and similar pattern to what has previously been presented in radiographic foot osteoarthritis using the LFA.

With the exception of the 1st metatarsophalangeal joint and the 1st cuneo-metatarsal joint, osteoarthritis was shown to have higher prevalence in the left foot joints. This is a surprising finding, as results would normally be expected to be higher prevalence in all right foot joints, in particular, the 1st metatarsophalangeal joint. Limb dominance is also most prevalent in the right lower limb which provides an understanding of the majority prevalence in the right foot joints. As the dominant lower limb is responsible for initial acceleration in the gait cycle, it is likely that these forces are partially responsible for the higher prevalence in that limb among the general population. However, this is an assumption as no analyses were conducted at this stage to determine associations or cause and effect. Sadeghi et al. (2000) explained the complexities of limb dominance, and how consistency and agreement between research studies is low. Data on limb dominance were collected in the year '23' study, however, due to the heterogeneity (use of differing methods and inconsistent data recording), it was decided to exclude the use of this data even following the data cleaning process. This was in part due to the quality of data, but also due to the neurological complexity of limb dominance, resulting in the decision that this information was of limited value as an inclusion.

Small differences were found in joint space narrowing between feet, and between features in all joints with the exception of the talonavicular joint. The latter (TNJ), demonstrated no ungradable joints whatsoever with a low prevalence in the alternative feature of osteophytic change (left foot 4.1%; right foot 3.7%). The discussion on ungradable joints is further expounded in Chapter 4 (section 4.6.), however, this data provides an insightful description as to how osteoarthritic features are distributed at the level of joint projections and in terms of the individual score and subsequent grading.

Noteworthy is the 2nd CMJ in terms of prevalence, which was found to be highest of all joints for both feet when considered individually and as a combined presence with radiographic osteoarthritis (person level). The results of the 2nd CMJ also loosely support the discussion by Menz et al. (2009) of the high proportion of bilateral cases in the 2nd CMJ as study data were found to be very similar prevalence. However, the results should be interpreted with caution as paired bilateral presence in this joint was not considered in the presented data, although the data by Menz et al. (2009) indicate paired data due to the particularly high prevalence of rOA in this joint. The difference between the paired prevalence of radiographic osteoarthritis in the 2nd CMJ and the next most prevalent joint (1st CMJ) of both feet was 21.1%. As the 2nd CMJ prevalence of rOA was particularly high and demonstrated a large percentage interval with the next most prevalent joint, it suggests the result was anomalous.

Perhaps the most interesting result, however, was the prevalence identified according to radiographic feature. When features were considered separately across all joints, the 2nd CMJ was considerably more affected when demonstrating presence of osteoarthritis in joint space narrowing. This is in no way surprising, as the 2nd CMJ was anecdotally identified as the most difficult joint to assess for joint space narrowing due to its central positioning in the midfoot where many structures created noise when trying to identify the joint due to apparent overlapping of osseus structures. Further to this, the work on appropriateness in Chapter 4 revealed the highest proportion of ungradable joints as being within the 2nd CMJ.

For the majority of joints in this study, joint space narrowing (diagnosis based, from ‘0’ or ‘1’ to ‘2’ or ‘3’) was found to be higher than osteophytic change suggesting that joint space narrowing was the more sensitive radiographic feature. However, it is accepted in the literature that both features should be used in diagnosing radiographic foot osteoarthritis (Arden and Nevitt 2006). The generally higher prevalence of the joint space narrowing radiographic feature (compared to osteophytic

change) links to findings highlighted in Chapter 4, that perhaps the joint space narrowing was less sensitive in the first metatarsophalangeal joint by relative comparison to the other joints assessed using the LFA.

5.9.2. Prevalence of foot pain

The prevalence of foot pain experienced at any time in the last year was established as 30.5% and that which had existed in the past month as 20.0%. Additionally, it was found that the responses of participants in answering questions about foot pain were consistent, and furthermore, that around two thirds (64.6%) of participants who had answered positively to single questions about having ever had foot pain, had experienced the pain in the past month.

No other published work was found relating to ever having had foot pain which was marked according to a foot manikin, as such it was not possible to make any comparison. However, data provided important novel research regarding the self-reported lifetime experience of foot pain among women aged 60 to 91. Combined joints with combined projections demonstrated 24.4% prevalence of foot pain in both the left and right feet. When comparing the combination of joints between projections, the right foot demonstrated higher prevalence of foot pain in the dorsal view. However, the opposite was true in the plantar projection. Overall 30.5% of participants were found to have foot pain in any region of the foot, in either foot and either view (dorsal or plantar). This was lower than expected given the prevalence of foot pain among the general population (men and women) which was found to be 24% through systematic review of the literature (Thomas et al. 2011). It is possible that this level of data from the participants is limited by recall bias and the inability to recall experiences of foot pain from previous years.

5.9.2.1. Generalised Foot Pain (Gen.FP)

The only research known, with relevance to this thesis, which recorded the same or a similar variable was by Munro and Steele (1998), which identified 53% of women over the age of 65 to respond positively to having ever had foot pain. Further information from this question was requested of the participants where participants were asked if their foot pain had changed over the last six years if they had ever experienced foot pain in the past. The prevalence of a change in foot pain status was found to be 76.8% (n=73; N=95; missing n=2) in the survey conducted by Munro and Steele (1998). This question may have been limited by difficulty in interpretation but demonstrates that for most older women who have experienced foot pain in the past, their pain experience does not stay constant but has altered in some way.

The overall prevalence of foot pain according the shaded MFPDI manikin was found to be 20.0% (Table 29). This is comparable to the current body of research in foot pain. Hill et al. (2008) identified foot pain in 17.4% of participants who shaded pain on a foot manikin. The association with gender also provides meaningful information; men had a prevalence of 15.1% (OR 1.00) and women had a prevalence of 19.6% (OR 1.38; CI 95%; P value 0.001). Despite describing the data collection of foot pain according to a marked foot diagram, no prevalence result was presented by Dunn et al. (2004) other than 14.9% pain in the ankle region by this method. Further to this, Garrow et al. (2004) found a similar prevalence of 24% (n=444) to have foot manikin identified foot pain lasting more than one day in the last month.

Participants were asked a single question investigating if they had experienced foot pain in the past month for one day or longer, which produced a prevalence of 64.6% (N=99; n=64).
This is a similar prevalence to Garrow et al. (2000) who used MFPDI-17 parameter where the selection of one item indicated prevalence of foot pain to establish a prevalence of 63.8% (N=387) foot pain among participants. Also of note, was research by Thomas et al. (2004) who found pain in any region of the body in the last 4 weeks to be 66.2%. This would therefore suggest that, perhaps, foot pain was recorded as being particularly high among women in the Chingford study.

Generalised foot pain was found to be low in both feet from the anterior (front) and posterior (back) aspects of the feet. Research has described pain in various areas of the body, however, as described in Chapter 2, the foot has often been neglected in the presentation of this research. The generalised foot pain prevalence in this study is considerably lower than that established in any other identification of foot pain (foot specific shaded foot pain manikins and single foot pain questioning) with the exception of clinician diagnosed foot pain (MFPDI manikin diagrams and single closed questioning of foot pain). The consideration of factors affecting pain is important, particularly as participants were not directed specifically to the foot, but the variable of interest was part of a multivariable question whereby pain was identified at any area of the body. Stoicism or previous experience of pain could be an attributable cause of the apparent low prevalence of Global Foot Pain whereby pain (in this case foot pain) is not recognised (as previously discussed in chapter 2). Furthermore, it may be the case that pain recognition among participants is based upon a hierarchy of severity. That is, the more severe the pain, the more likely it is to be recognised. Therefore, if foot pain is of lesser severity, relative to other parts of the body, participants may either chose to ignore its presence (stoicism) or may unknowingly (or subconsciously) ignore (severity hierarchy) its presence.

The NorStOP study by Thomas et al. (2004) found a generalised foot pain prevalence of 22.9%. It is possible that in the Chingford study, the ankle was confused with the foot section by participants as guiding lines to regions of the body were not included in the diagram, therefore regions of the body were not defined for the participants. Foot pain (combined left and right views) was found to be 5.7% (n=18; N=315) with ankle pain found to be 4.4% (n=14; N=315) with the further combining of ankle and foot pain providing a prevalence of 7.6% foot (and ankle) pain (n=24; N=315). It can be concluded that generalised foot pain was lower than expected among the Chingford women; this emphasises the disparity between foot pain where it is non-specific (generalised foot pain) and specific to the foot (Global Foot Pain).

5.9.2.2. Global Foot Pain

The Manchester Foot Pain and Disability Index (MFPDI) was not originally purposed with the intention of evaluating each individual item. Definition 'A' denoted by Menz et al. (2007) was used to present data whereby all participants selected one item out of the index (MFPDI) as being 'most days'. However, it provides an insightful breakdown of pain among the Chingford cohort of older women and is comparable with work by Menz et al. (2011) in the North West Adelaide Health study which can be seen in Appendix 7. The studies are effective studies for descriptive comparison as a means of external validation. The study by Menz et al. (2007) presented results stratified according to gender, which removes the limitation that female only participants in the Chingford study may have created. Additionally, a similar number of participants were analysed in both studies with a difference of 17 participants (12.6% less in the Chingford study than in the Adelaide based study). Menz et al. (2007) also stratified according to age, with the most comparable group being aged 71 to 90 in Menz et al. (2007), whereas the Chingford group ranges from 69 to 91. However, this analysis involved a smaller group of participants (N=54). Pain was found to be lower in percentage prevalence in the Chingford based study in every item of the index with the exception of three items;

(1) I catch the bus or use the car more often

(2) I need help with housework/shopping

(3) I feel self-conscious about the shoes I have to wear

NB: All items are a result of participants experiencing foot pain

The second item relating to participants' need for help with housework or shopping was a small difference of 2.4% between studies, where the Australian study was stratified according to female gender. More to the point, a 2.4% difference was also found to exist in the Australian population

when comparing participants stratified according to age and gender, therefore age did not appear to affect this item. As it is a small difference, consideration of this result could be deemed negligible. However, the result is plausible as participants in the Australian based study were recruited from a community based dwelling cohort where it is likely shops were more accessible compared to the Chingford participants in London, who did not live as a community. Furthermore, this was the only item to display a higher prevalence among the Chingford based participants experiencing this consequence of foot pain on 'most days'.

The item relating to using motorised transport showed the greatest difference compared to the women in the Australian study, with 14.3% higher prevalence among the Chingford women. This did not seem to be affected by age with a 0.9% difference between participants stratified according to age. It is possible that efficient transport links across London and the easy accessibility to buses for UK citizens over the age of 60 had an important influence on this result. It is also possible that the community dwelling participants from the Australian population may have had better access to amenities and therefore were less likely to use public transport.

Finally, the prevalence of women feeling self-conscious about their footwear due to foot pain was higher in the Australian study by 4.9%. The effect of age on this item in the Australian population was that more participants of younger age categories were self-conscious about their footwear compared to the age group of 71-90 years, with a difference of 9.4% between participants stratified by age. Therefore, had the study been designed to include women only of the older age group (71-90 years), it is possible that the prevalence for this item may have been higher in the Australian study than Chingford study. Of note, participants in the Chingford study were less self-conscious about their feet than the participants in the Australian study despite being more self-conscious about their shoes. This is not surprising due to the known anecdote of fashion conscious attitudes in London and confirmed through recent work by Bowen et al. (2016) where the same Chingford cohort were found to regularly wear heels for long periods. Furthermore, this association of the time spent in heels decreased with increasing age which the hypothesis that self-conscious footwear beliefs were replaced in favour of wearing comfortable footwear to reduce foot pain.

Pain prevalence according to the Manchester Foot Pain and Disability Index (MFPDI-17) was consistently lower among the Chingford based participants compared to the Australian based participants. This was consistent and the exception of three items to this prevalence pattern (lower in Chingford) can all be accounted for through the descriptive comparison. This may represent

possible cultural differences between the UK and Australian population, and may be further explained by one important methodological difference that participants in the North West Adelaide Health Study were all recruited as community-dwelling participants, where perhaps there is a higher recognition of pain perception through more frequently discussed common symptoms. Appendix 10 shows a direct comparison externally validating the work within the Chingford study with work by Menz et al. (2011).

5.9.2.3. Foot Joint Pain: Clinician diagnosed foot pain

The investigation of clinician diagnosed foot pain is in its infancy as it continues to be an area of little consideration. As an isolated example, the Boston MOBILIZE study (Eggermont et al. 2009) carried out investigation of clinician diagnosed pain through a 'musculoskeletal examination' which involved observation and movement of the hands, wrists, hips, knees and, unusually, the feet. However, data on the feet were reported based on how widespread pain was, the number of sites affected, or referred to the more generalised term of 'lower extremity pain' (Leveille et al. 2008; Leveille et al. 2009; Eggermont et al. 2009). Although the foot pain identified within this cohort would not create the ability to analyse associations with radiographic foot osteoarthritis, it does encourage discussion about the clinical relevance of clinician diagnosed foot pain, and in this case, through passive joint motion.

Currently, foot pain continues to be an under-researched area in need of more extensive and in-depth investigation. It is therefore not surprising that very limited research exists on clinician diagnosed foot pain. This therefore requires the exploration of broader concepts in the available research. In an article on multiple joint pain by Edwards et al. (2012), the 'squeeze test' was described as a means of identifying possible underlying joint inflammation when undue pain response was experienced. This was used as a test involving multiple joints simultaneously in the absence of swelling or inflammation. Although there is little research into 'positive squeeze' or 'motion palpation' tests, there is clearly a recognised value in the use of palpation or dynamic motion of joints to stimulate a pain response and the implication of associated symptoms of inflammation and clinician diagnosed pain, where pain is an indicator of pathology.

With such low prevalence of pain identified in clinician diagnosed pain, it can be said that it is not a sensitive measure of pain given that 20.0% of patients in study 2 identified current foot pain using self-assessed questionnaires. Interestingly, the protocol developed by Roddy et al. (2011) for the CASF study initially documented the inclusion of pain reported through physical clinical assessments, however, this was excluded in the subsequent publication and in light of the results of study 2 was

likely influenced by the test's low sensitivity to pain (Roddy et al. 2015). However, this prevalence is perhaps an area that should be considered in research, specifically as to why some patients will experience clinician diagnosed pain. It would be beneficial to investigate the clinical significance of this test as an indicator in joint health considering the complex nature of pain and challenges in establishing strong associations with pathophysiology (Arden and Nevitt 2006). This raises the question as to whether the clinician diagnosed pain involves patients from among those who identified foot pain or no foot pain through the MFPDI self-assessment. Until further research is carried out, however, it is understood that the key benefit as denoted by Hawker (2017) for physical examination specific to identifying pain is as a complimentary assessment to the self-assessment carried out by patients.

Further to this there are two important considerations resulting from the data. The first is that it is evident that clinician based assessment of foot pain does not accurately capture the foot pain described by participants through self-reported measures. The second consideration is that the data would suggest that as a result of this, foot pain is under-reported in a clinical setting when there is reliance on 'current' and 'clinician diagnosed' foot pain. Despite the fact that the data appears limited, it raises the important issue with foot pain that in a clinical setting, it is not adequate to rely solely on a clinician based diagnosis of foot pain to determine presence of foot pain in a patient. Of note, overall prevalence of clinician diagnosed foot pain (where both feet were combined) was found to be **3.0%** (n=6; N=200).

5.9.3. Radiographic foot osteoarthritis and co-existing pain

Global Foot Pain, with reference to disabling foot pain, established through participants identifying foot pain 'most days' for at least one item of the ten used (definition located in section 5.6.3.1.) was found to co-exist with radiographic foot osteoarthritis in 10.3% of participants. Compared to the findings by Roddy et al. (2013) of 12.6%, this further supports the validation of foot pain by the authors and validates the use of these methods of identifying disabling foot pain in the Chingford 1000 Women study. We can therefore identify that one in ten of the Chingford ladies had disabling foot pain with radiographic foot osteoarthritis.

For Global Foot Pain, specifically disabling foot pain, small differences were observed between prevalence estimates of isolated disabling foot pain (participants with non-descript presence of radiographic osteoarthritis) and disabling foot pain among participants with the presence of radiographic foot osteoarthritis. Differences exhibited between definitions of disabling foot pain with co-existing radiographic foot osteoarthritis were small, with a range of 0.4% to 3.2% across

established definitions sourced from the literature. It should be noted that the prevalence of radiographic foot osteoarthritis was found to be high (91.3%), so large differences were not anticipated. However, the small differences seen between studied participant groups were relevant to the understanding that disabling foot pain is not noticeably different among a UK population-based cohort of older women with radiographic osteoarthritis. This study is unique in presenting radiographic foot osteoarthritis in the context of clear and defined disabling foot pain.

Co-existing radiographic foot osteoarthritis and generalised foot pain identified as one item from the Manchester Foot Pain and Disability Index (shaded MFPDI foot manikin) was found to be 20.8%. In contrast to overall foot pain (shaded MFPDI foot manikin) found to be 20.5%, painful foot osteoarthritis was found to be 0.3% higher showing that only a small amount of pain was truly unrelated to radiographic foot osteoarthritis. This co-existence is comparable to the overall symptomatic radiographic osteoarthritis prevalence established by Roddy et al. (2013) of 16.7%. This difference of 2.3% is similar to the point that it validates the findings by Roddy et al. (2013) and also validates this research within the Chingford cohort. This supports the recognition that painful radiographic foot osteoarthritis exists in one in five of the general population by Roddy et al. (2013). It is unsurprising that the prevalence was marginally higher in the Chingford based study considering the inclusion was limited to female participants only, which is likely to increase the prevalence due to the recognised higher prevalence of radiographic foot osteoarthritis among women (Menz et al. 2009).

Foot joint pain (clinician diagnosed foot pain) and co-existing radiographic osteoarthritis was found to be present in 3.4% of participants. At present there are no known comparable data and this has provided a precedent for future research. It also provides a reference point for the diagnosis of patients with pain that can be identified in combination with radiographic foot osteoarthritis within a clinical setting. Further to this point, data on co-existence has brought into question the clinical relevance of this type of assessment for the diagnosis of painful radiographic foot osteoarthritis. It was established in section 5.9.2.3. that clinician diagnosed foot pain is not adequate for capturing foot pain and therefore it would be inappropriate to rely on this assessment for a diagnosis of painful radiographic foot osteoarthritis. This is an important consideration as health care professionals have traditionally carried out passive joint motion to diagnose foot pain as part of their musculoskeletal assessment of the foot. This validates the recent work by Gates et al. (2015) which excluded clinician diagnosed foot pain through passive joint assessment as it has shown a limited ability to capture painful radiographic foot osteoarthritis.

The only known allusion to the disparity between clinician and patient self-reporting of pathology is the reference to foot problems by Garrow et al. (2004). The discussion makes note of the lack of agreement between the clinician (observer) and patient self-reporting (respondent). However, it is interesting to note that this lack of agreement was attributed to the participants' poor ability to recognise their own foot problems. It should, however, also be noted that self-reporting of major conditions or illnesses such as cancers by participants was described as accurate when compared to histopatholoy reports, but to a lesser degree in other more complex conditions such as myocardial infarction and cerebrovascular accidents (Colditz et al. 1986). This holds true to the concept that self-reported problems such as foot problems are poorly reported, however it is contrary to the concepts understood in foot pain through the lack of agreement between reporting of clinicians and patients.

5.9.4. Strengths and potential limitations

A key strength of this study is that it is a large population based prospective cohort study representative of middle and older-aged women (aged 45-64) recruited from a general practice in North-East London, UK. Potential limitations are outlined in two parts, those requiring more detailed discussion, and biases that may have influenced the results. A list of the biases that may have impacted the study can be found in Appendix 4 where definitions, applications to the study and the potential impact on results have been detailed.

The first limitation that exists relates to the type of pain data that have been collected. The foot pain, like much of the preceding research, is non-specific to joints and so, whilst timing and frequency are aspects identified among participants, the source or cause of pain is not differentiated. Although not essential for investigating this association and not uncommon in research studies, this does affect the accuracy of the data collected if considering foot pain specific to joints.

The second limitation that exists is that the demarcated sections on the diagrams which relate to the foot do not correspond with relation to areas such as 'first digit' and 'first metatarsal'. This necessitates the combining of sections, as the demarcations of foot pain areas according to the Manchester Foot Pain and Disability Index often lie on the joint margins, and do not correlate well when considered with specific joints.

Foot pain was also considered in terms of clinician diagnosed foot pain. Clinician diagnosed foot pain data are a novel contribution and unique to this research. Specific to the foot, clinician diagnosed foot pain remains unreported in the research. A positive response to foot pain was recorded where patients said 'yes' to having a pain experience when questioned following the passive motion of each joint by the MPhil student. Clinician diagnosed foot pain was investigated as part of a screening system whereby 'red flags' were identified and escalated to the appropriate professional for management of the conditions. Pain, as well as heat and swelling, was among the 'red flags' during the physical assessment. However, this was not primarily intended for the purpose of data collection.

Finally, Global Foot Pain using a full body manikin was included in the year '23' questionnaires for participants to identify pain in their body as a self-reported measure. For this research, the specific interest was on the relevance of foot pain in the context of the whole body and how this differed from foot specific questioning on pain (Figure 13).

Validated foot manikins (or diagrams) were sourced from Otter et al. (2010) (Figure 11 and 12) and Manchester Foot Pain and Disability Index (MFPDI) with the relevant permissions being sought. As combinations of foot sections on the diagrams were used for looking at associations between radiographic foot osteoarthritis and foot pain rather than relying on individual sections, it was anticipated that this would make little to no difference. It is accepted, however, that a limitation may exist in using these diagrams interchangeably in the data analysis as there are minor differences which may affect the accuracy. However, both diagrams are considered valid research tools and therefore any compromise of accuracy is between diagrams rather than due to their ability to measure foot pain appropriately (Otter et al. 2010). This may give rise to the possibility of systematic error as a different ordering format was used between versions. The initial diagram (Figures 15 and 16) has less detailing and the format is not as clear in identifying plantar or dorsal surfaces of the feet, meaning that participant error in the recording of data could occur.

Non-responder bias: Data have not yet been collected for the participants of the Chingford 1000 Women study who did not attend the clinical visit in year '23'. There is intent to collect these data using telephone questionnaires to enable comparison and observation of any bias between the responder and non-responder groups. However, data can be provided for those that did not attend x-ray (N=78) or return completed pain questionnaire booklets (N=22), to consider any response bias within these subsets. Between Year 20 and '23' follow up, the highest recorded number of deaths

occurred where 65 participants passed away, 12.6% of the participants seen at the previous Year 20 follow-up (6.5% of the total number of participants from baseline).

5.10. Conclusion

Data were collected and analysed for the Chingford 1000 Women study year '23' visit to establish prevalence of radiographic foot osteoarthritis, foot pain and the co-existence of both. Radiographic osteoarthritis among older women was found to be high but this was consistent with the current body of evidence. Foot pain was also found to be consistent with current literature and novel data on clinician-diagnosed foot pain were presented demonstrating that this is not representative of patient-reported foot pain.

The exploration of the prevalence of radiographic foot osteoarthritis and co-existing foot pain was an important one. The findings from this study provide external validation of previous research whilst also highlighting the number of ongoing foot pain definitions, particularly when using the Manchester Foot Pain and Disability Index. Finally, the novel research has created an important and key discussion in how research in epidemiology specific to osteoarthritis in the foot should move forward.

5.10.1. Key Points

Prevalence of co-existing foot osteoarthritis and foot pain

Key points

- Osteoarthritis is highly prevalent among older women in the general population.
- Approximately 3 in 10 older women have experienced foot pain at some point in their life.
- When rOA was stratified, general increases in prevalence could be seen for increased age and increased BMI.
- Around one fifth of women had co-existing foot pain with rOA in the feet.
- Around one tenth of women had co-existing disabling foot pain with rOA in the feet.

5.10.2. Summary

This chapter has investigated the cross-sectional prevalence of radiographic foot osteoarthritis, foot pain using various outcome measures, and the co-existence of both in a single cohort of UK women. The next chapter will explore the natural history of asymptomatic and symptomatic radiographic foot osteoarthritis and of foot pain with incidence and prevalence change presented making use of the longitudinal study design. This will help in understanding the importance of pain as a clinical indicator of future radiographic osteoarthritis among women.

Chapter 6: Study 3: The natural history of radiographic foot osteoarthritis and co-existing foot pain UK among a cohort of older women.

6.0. Introductory chapter summary

In chapter five radiographic foot osteoarthritis was confirmed as highly prevalent (91.3%) in a cross-sectional sample of older women recruited into a cohort study from the general population, and that radiographic foot osteoarthritis with co-existing foot pain was moderately prevalent (20.8%). In order to determine the clinical relevance of asymptomatic radiographic foot osteoarthritis and optimise the management of foot symptoms associated with osteoarthritis it is only appropriate to progress to the investigation of the natural history and progression of radiographic osteoarthritis within the feet over time. Chapter six forms the final study of the thesis in which changes in the presence of radiographic foot osteoarthritis and its association with co-existing foot pain are investigated over time and the results are presented accordingly. Discussion of the results with exploration of strengths and limitations is provided, with key themes and points concluding the chapter.

6.1. Introduction

There is a growing body of evidence that details the prevalence of radiographic osteoarthritis within the feet, as well as the prevalence of foot pain (Roddy et al. 2015; Abhishek et al. 2010; Wilder et al. 2003). Whilst these investigations consider the prevalence of radiographic foot osteoarthritis and the prevalence of foot pain, data generated from longitudinal study designs are rare (Wilder et al. 2005). Of note, the most important study considering both radiographic foot osteoarthritis and foot pain focused on individuals recruited with foot pain, and little evidence exists demonstrating co-existing radiographic foot osteoarthritis and foot pain among a general population (Roddy et al. 2015). Thus the clinical relevance of symptomatic and asymptomatic foot osteoarthritis remains relatively unknown.

Numerous studies have been carried out on the hip and knee exploring the incidence of osteoarthritis through a longitudinal study design (Cicuttini et a. 2004; Bloecker et al. 2015; Amstutz and Le Duff 2016). However, no research in radiographic osteoarthritis is known to exist with a particular focus on the feet using a longitudinal study design. Wilder et al. (2005) highlighted the absence of literature presenting co-existence of foot pain and radiographic foot osteoarthritis, specifically of the 1st metatarsophalangeal joint. Roddy et al. (2013), in the justification for their research, identified that relative prevalence of radiographic osteoarthritis and co-existing foot pain

was not known to any extent within the general population. Kalichman and Hernandez-Molina (2014) identified the need to move the current body of knowledge on radiographic foot osteoarthritis forward from small case-control studies to population studies considering risk factors. This is particularly relevant to the work of this chapter, considering the important and under-researched area of co-existing foot pain with radiographic foot osteoarthritis.

Typically, the clinical method of assessment is to assess patients following symptoms such as pain. However, the prevalence of radiographic osteoarthritis with and without pain is unknown over time. These results will increase understanding of radiographic foot osteoarthritis and in time may lead to improved, targeted and more directive treatments. Therefore it is clinically important to understand the natural history of radiographic foot osteoarthritis from baseline (year 6) in the context of foot pain as the outcome at follow-up (year '23'). This will be helpful in understanding the importance and future relevance of researching radiographic osteoarthritis early on for determining target populations and potential preventative measures. Determining target populations with preventative measures in the future may also lead to the reduction of pain in older patients in the future.

In the previous cross-sectional study investigation (Chapter five) it was reported that radiographic foot osteoarthritis with co-existing foot pain (symptomatic radiographic foot OA) was lower than radiographic foot osteoarthritis without foot pain (asymptomatic radiographic foot OA). To the researcher's knowledge, no studies have addressed the question of whether investigation of the natural history of radiographic foot osteoarthritis would provide further insight into the clinical relevance of radiographic foot OA.

It is clear from the literature that incidence of radiographic foot osteoarthritis is unknown, and this chapter therefore explores the prevalence and incidence using two time points among matched participants (baseline and 17 year follow-up). Finally, the change of radiographic osteoarthritis according to the LFA will be presented to understand the types of radiographic joint changes that occur and recognise any patterns existing in the data.

RESEARCH QUESTION

What is the natural history of asymptomatic and symptomatic radiographic foot osteoarthritis among a UK population-based cohort of women over a seventeen year period?

6.2. Aims and objectives

Aim: To show the natural history of radiographic foot osteoarthritis, foot pain and the co-existence of both characteristics in a UK population-based cohort of older women over time, from middle age to older age.

Objectives:

- Investigate the change in prevalence of radiographic foot osteoarthritis over a 17 year time period (year 6 to year '23') in a UK population-based cohort of older women.
- Explore the natural history of radiographic foot osteoarthritis in the first metatarsophalangeal joint, with co-existing foot pain over time.

6.3. Methods

6.3.1. Study Design

A longitudinal, 17 year cohort study design was used in which a sample of foot radiographs taken from a UK population-based cohort of older women at year 6 (from baseline), were assessed for radiographic foot osteoarthritis and were reassessed at year '23' for radiographic foot osteoarthritis seventeen years after the initial baseline visit for foot x-rays. This will be considered as natural history using three means of analysis, the prevalence at two time-points, the change between baseline x-ray (year 6) and follow-up (year '23') and the incidence of 1st MTPJ radiographic osteoarthritis.

The study focused on the natural history, observing phenomena in longitudinal data through making use of a longitudinal prospective cohort study. Year '23' was the first year to consider foot characteristics, although previous foot x-rays were captured at year 6 and foot related variables were historically collected.

Prevalence and incidence are both means of presenting the natural history of disease in a population. Bonita et al. (2006) consider incidence to be the rate of occurrence of new cases within a specific time period, whilst prevalence is the frequency of a disease in a population at one time point. The natural history is presented using year 6 (collected in 1995) and '23' x-ray data (collected in 2014-15) using the dorsoplantar projection only, due to the lack of availability of lateral projection x-rays in year 6. Year 6 and '23' foot x-rays were evaluated for osteoarthritis using the technique established in Section 4.6.

Foot pain was considered on a foot level, as greater detail was not available on a joint or region specific detail for year 6 data. Prevalence of radiographic osteoarthritis and of foot pain is presented at the two time points in keeping with the natural history. Incidence is presented by removing participants with presence of radiographic osteoarthritis in the foot at baseline and calculating new cases of radiographic osteoarthritis in accordance with the methods used by Leyland et al. (2012) and Thorstensson et al. (2009) for other incidence studies.

6.3.1.0. Participant recruitment

In this study, data from participants were sourced from year 6 (considered as the thesis study baseline) and year '23' (considered as the follow up visit). Participant recruitment, inclusion and exclusion criteria for year '23' is described in detail, section 3.8 table 4, chapter 3 as similar principles of prevalence were used and advanced upon. For year 6, foot radiographs were sourced from established data collected as part of the Chingford 1000 Women study (section 3.6 Chapter 3). For this investigation all radiographs available from the year 6 dataset were assessed for prevalence of foot OA.

6.3.1.1. Timescale

Study 3 incorporated data from both year 6 and '23' of the Chingford 1000 Women study, the ethical approval processes of which are described in the preceding chapter 3 section (3.5). Heterogeneity exists between the two years of study baseline (year 6) and the returning visit (year '23'). The heterogeneous characteristics included having only one projection (dorsoplantar) in year 6 dataset and the x-rays being recorded in a different format (plain film and electronic).

The data for year 6 were carried out in 1995 by the previous study investigators. The data for year '23' were collected by the researcher (PMc) between November 2013 and July 2015 (Chingford year '23'). Analysis of the data took place between November 2012 and September 2016. All references to 'baseline' and 'follow-up' in this chapter refer to the baseline of radiographic foot assessments (year 6) and follow-up of radiographic foot assessments unless otherwise stated.

6.2.1.2. Selection criteria year 6 and '23'

Inclusion criteria

- All participants that had complete dorsoplantar foot radiographs at baseline
- All participants who also had complete foot radiographs in the dorsoplantar projection at follow-up.

Exclusion criteria

- Participants with foot radiographs that were damaged or unreadable or in some cases damaged and unreadable.

6.3.1.3. Sample size

Due to the unique design of the study considering painful radiographic osteoarthritis in a UK population-based cohort of older women (not defined by the presence or absence of pain), there was no known available research on which to base a power calculation for the consideration of foot osteoarthritis and co-existing foot pain. To establish power, a study of the knee by Leyland et al. (2012) was used to carry out a sample size calculation. This was the most suitable study as the period between visits was similar to the thesis project, and it similarly considered two time points of prevalence in addition to incidence. Although little can be extracted from this calculation in terms of meaningfulness, it ensures the appropriate number of participants are analysed and, to the best of our knowledge, that statistical power can be achieved within the results described by Bowling (2009). Calculating a sample size with a 5% level of significance using the reference population as N=561, it was considered that 36 participants would be required to achieve power. The sample size for this study was deemed appropriate to establish power on the basis of usable paired participants (N=197) with data extracted from year 6 and '23' of the Chingford 1000 Women study.

Calculating the sample size ensured that statistical power could be achieved and thus provide meaningful results. The sample size was calculated using the following equation;

$$n = \frac{Z^{2\frac{a}{2}}\, p(1-p)}{d^2}$$

p = proportion of interest

z = confidence level

d = margin of error

a = confidence interval

The sample size required to achieve power was established (Section 5.4.2.) as 181 participants based on a sample of 561 from the reference population with a longitudinal design (Leyland et al. 2012)

and with an expected proportion of 0.02 (from the 2.3% incidence of rOA). This sample size was achieved using a 5% confidence interval (margin of error) with a confidence level of 95%. Having established a population of 36 participants who attended x-ray, this population is an appropriate size to establish statistical power of the results. All participants who had paired foot radiographs at both year 6 and '23' were included in this study (193) which surpassed the requirement to establish statistical power within the sample.

6.3.2. Data collection

6.3.2.0. Assessment of radiographic foot osteoarthritis for longitudinal analysis.

As can be seen in figures 18, 19 and 20, there is a disparity in the methods of diagnosing radiographic 'foot' osteoarthritis and radiographic 'knee' (or 'hip') osteoarthritis. The problem presented relates to the additional number of conditional variables that constitute a definition of radiographic foot osteoarthritis. Where the knee is dependent on one joint having presence of either radiographic feature (osteophytic or joint space narrowing) in one radiographic projection, the foot is dependent on the presence of either radiographic feature, in any one of five joints, in either dorsoplantar or lateral projection. The approach to defining radiographic foot osteoarthritis could therefore be considered as multifaceted and multidimensional when compared to the standardised methods observed in diagnosing hip or knee osteoarthritis.

Furthermore, the diagnostic methods of hip and knee osteoarthritis rely solely on the presence of radiographic change in a single joint using a single radiographic projection (Kellgren and Lawrence 1963; Ingvarsson et al. 2000). Referring to radiographic 'foot' osteoarthritis according to the LFA predetermined joints could be considered similar to referring to radiographic 'lower limb' osteoarthritis on the basis of presence of radiographic change in the hip or knee joint. The diagnosis of 'foot osteoarthritis' incorporating multiple joints with the LFA, may be more appropriately referred to as 'polyarticular evaluated radiographic foot osteoarthritis'. The summary of all variables constituting 'polyarticular evaluated radiographic foot osteoarthritis' can be seen in figure 18.

Therefore in the analysis, individual joints should be considered in isolation using a single projection as with the standardised hip and knee diagnoses (Figures 19 and 20). All predetermined LFA were therefore considered whilst also considering joints in terms of the number of ungradable joints to understand which joints were more difficult to evaluate. The reason for doing this was due to the inevitability of the ungradable joints affecting the comparable prevalence if there was a notable difference, and therefore affecting the interpretation of results. As the natural history was considered within the thesis, it was established that a 'polyarticular evaluated' approach was not

appropriate given the preceding work on natural history of osteoarthritis, and it was therefore important to consider one joint. In isolating the single joint, the most gradable joint was selected to provide the most reliable presentation of results demonstrating radiographic change. This was carried out by selecting the joint with the least joints considered to be ungradable, and the participants with joints considered to be ungradable at either year 6 or '23' data were excluded from the analysis. Figures 19 and 20 show the single projection, single joint approach that was employed in the preceding research on the natural history of osteoarthritis that was similarly applied to the foot (using the framework of the LFA as in figure 18) to establish the natural history of osteoarthritis, which was novel to research in radiographic foot osteoarthritis.

Figure 18 Diagnosis of multifaceted radiographic foot osteoarthritis in multiple projections

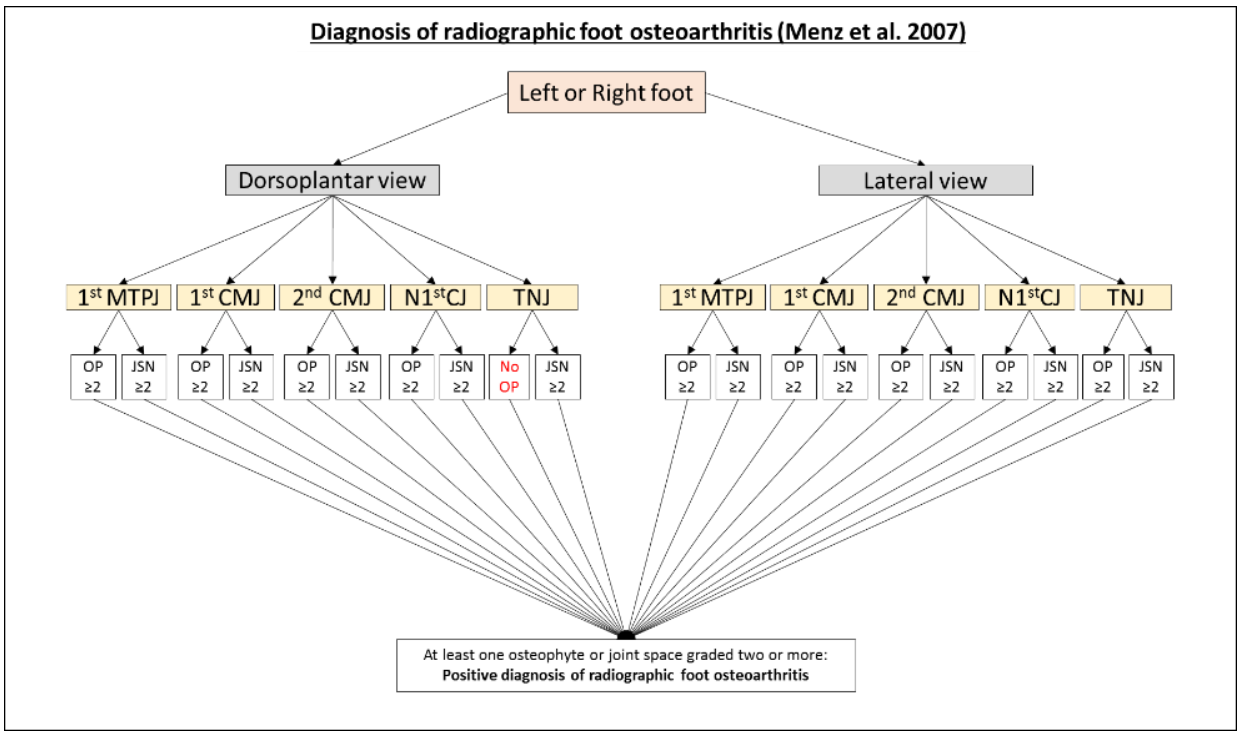


Figure 19 Diagnosis of radiographic knee osteoarthritis

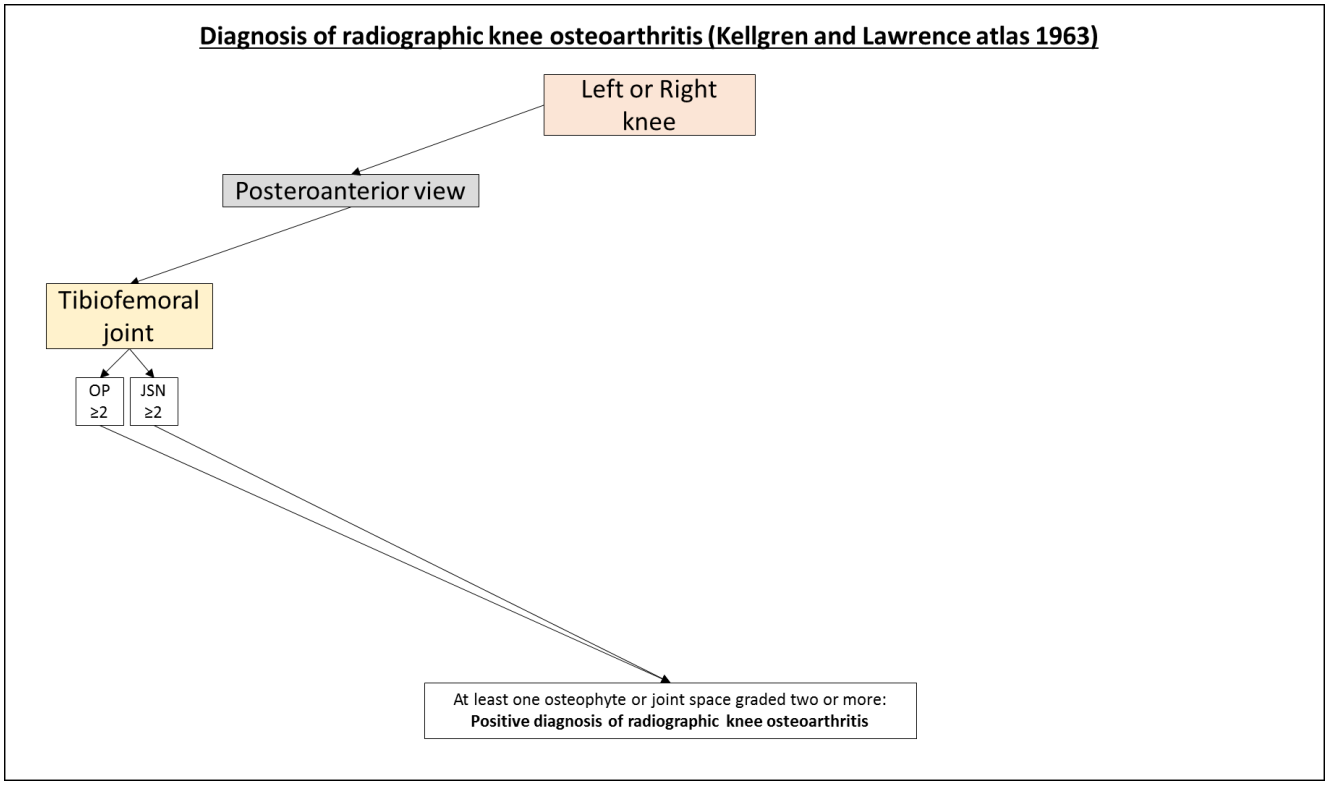
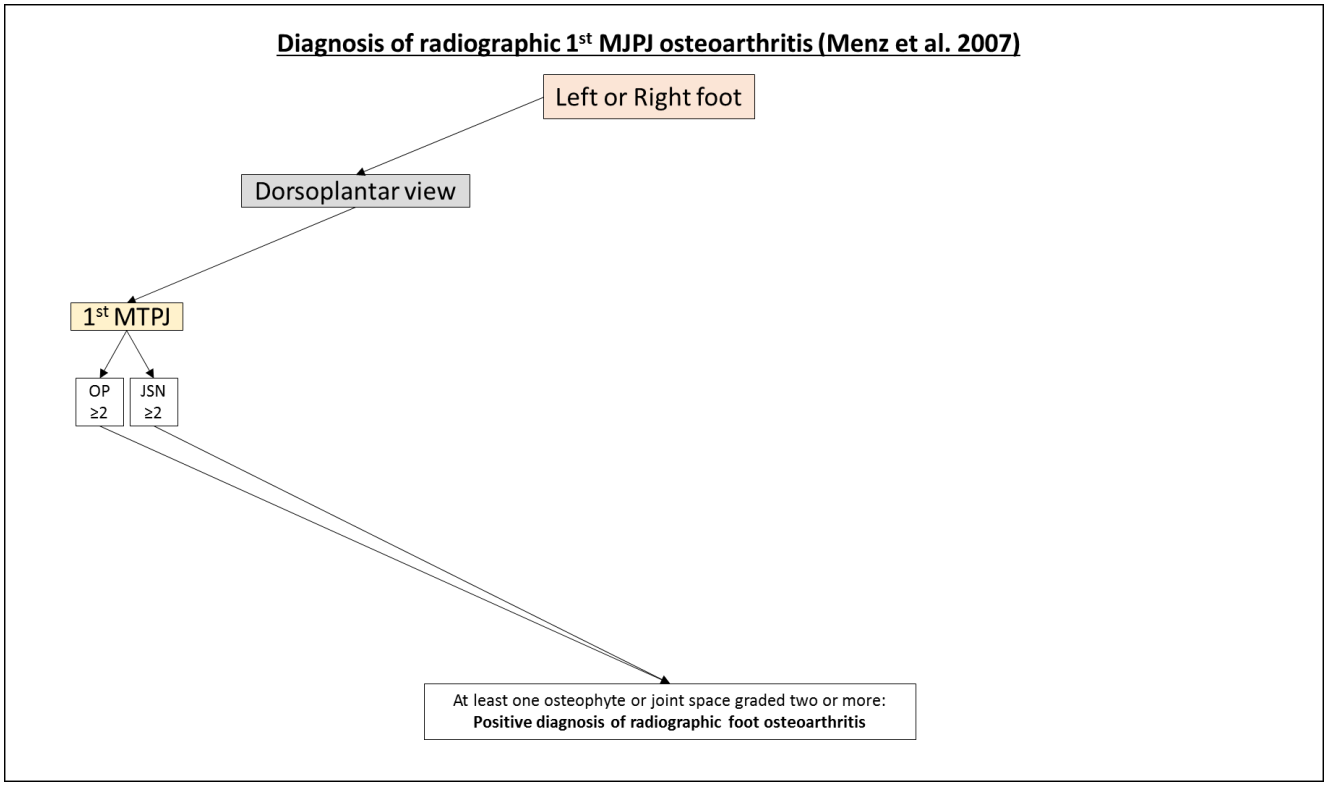


Figure 20 Diagnosis of radiographic single joint osteoarthritis in a single projection



6.3.2.1. Procedure for identifying radiographic foot OA

The procedure for foot x-rays for year '23' is documented in section 5.3.6. chapter 5. For year 6, foot x-rays had been taken following the same standard procedure, however these were available in dorsoplantar views only.

6.3.2.2. Assessment of radiographic foot osteoarthritis

The definition of radiographic foot osteoarthritis is described in detail in section 3.6., chapter 3. That is, foot radiographic osteoarthritis is defined by the LFA scoring method (Menz et al. (2007) as present if a score of 2 or above is documented for either osteophytes or joint space narrowing, in either projection. Only the dorsoplantar projection was collected at year 6 and so for consistency, the lateral projection was excluded from the year '23' dataset for the analysis of longitudinal data.

As highlighted in chapter 4, the approach to defining radiographic foot osteoarthritis according to Menz et al. (2007) is multifaceted and multidimensional (or dual radiographic projections) when compared to the standardised methods observed in other research for diagnosing hip or knee osteoarthritis. The methods of other research studies rely solely on the presence of radiographic change in a single joint with a single radiographic projection (Kellgren and Lawrence 1963; Ingvarsson et al. 2000).

Therefore, for the purposes of this investigation of the natural history of radiographic foot osteoarthritis the focus will be on one joint in a single projection. The 1st MTPJ was selected in chapter 4 as the joint to be investigated as it had the most reliable scores for determining the prevalence of radiographic foot osteoarthritis (identified as having the least ungradable joints).

As part of the evaluation of the 1st MTPJs, changes in radiographic osteoarthritis are presented according to each foot and according to the grade of osteophytes and of joint space narrowing. It was not possible to capture the individual scores of each joint when the left and right foot were considered together. However, prevalence was expressed according to the diagnosis of radiographic osteoarthritis when the left and right foot were considered together.

6.3.2.3. Assessment of foot pain

The case definition for foot pain assessed in year '23' and used for prevalence and incidence is described and discussed in detail in sections 3.6. and 6.2.1, chapter 3 and chapter 6. Overall foot pain was established for both year 6 and year '23'. The year '23' definition used directed participants to shade a foot manikin demonstrating where they had experienced foot pain lasting more than one

day in the past month. Individual regions were dichotomized to change the data into binary variables (more than one being converted to presence) and dichotomized to achieve person level foot pain prevalence. However, year 6 foot pain used to present prevalence of foot pain was relevant to foot pain in the last year and to additional symptoms of stiffness and swelling. The data were recorded as free text and were converted to binary variables to establish prevalence of left, right and either foot for pain. These variables were the only foot pain variables collected at year 6 and questions were asked in the following format;

- 'Left foot: Have you had any episodes of pain, stiffness or swelling in the past year?'
- 'Right foot: Have you had any episodes of pain, stiffness or swelling in the past year?'

No self-reported foot pain variables between year 6 and '23' were directly comparable. However, year 6 would not have the same accuracy as the year '23' data (a directive and validated pain symptom only variable) which were only used as a descriptive comparison for the study. As year '23' was required to describe the natural history, the variable chosen needed to reflect the most accurate and valid foot pain variable, and was used for the best estimation of this result in the general population.

6.4. Statistical analysis

Statistics used were a continuation of those used in chapter 5 (section 5.4.) and can be referred to as the means of presenting data in chapter 6. Additional work and clarification is given below for areas that are not explained in chapter 5. The data were collected and entered into IBM SPSS 22.0 Chicago software to produce the tables and graphs presented throughout the chapter, showing different presentations of the data collected on radiographic foot osteoarthritis and foot pain, individually and combined. All analysis carried out was observational providing descriptive statistics.

Prevalence for both radiographic foot osteoarthritis and for foot pain were assessed by calculating percentages by dividing the number of subjects with radiographic osteoarthritis at each visit by the number of subjects with x-rays at both year 6 and year '23'. Natural history was assessed observing structural change of osteoarthritis (irrespective of foot pain) by calculating percentages of participants that changed from presence to absence or absence to presence of radiographic osteoarthritis between year 6 and year '23'. This included both the worsening and improvement of both radiographic features of osteoarthritis taken from the total number of possible participants in the analysis.

Incidence was analysed by removing participants with presence of radiographic osteoarthritis in the foot from the total participants analysed. The percentage of participants that developed radiographic 1st metatarsophalangeal joint osteoarthritis were then calculated at year '23' to establish those with no radiographic osteoarthritis in the foot at year 6. The percentage was presented as part of the descriptive analysis instead of a rate-per-year due to the relatively small sample size. Additionally, natural history was calculated by identifying the prevalence of participants who had presence and absence of radiographic foot and 1st MTPJ osteoarthritis among participants at baseline who progressed to have pain at follow-up (Figures 21 and 22).

Figure 21 Natural history summarised: Prevalence of radiographic osteoarthritis presence with and without foot pain at baseline showing those who present with pain at follow-up

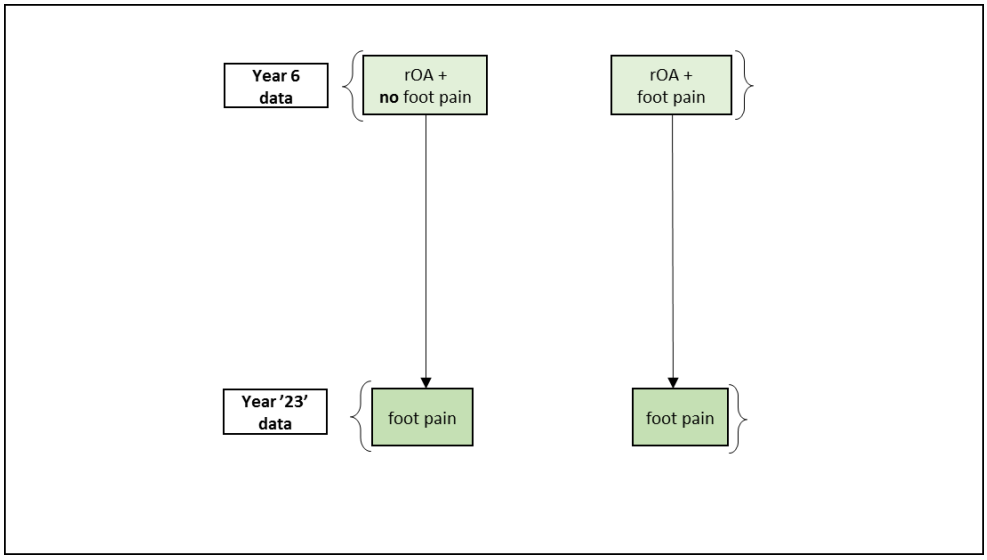
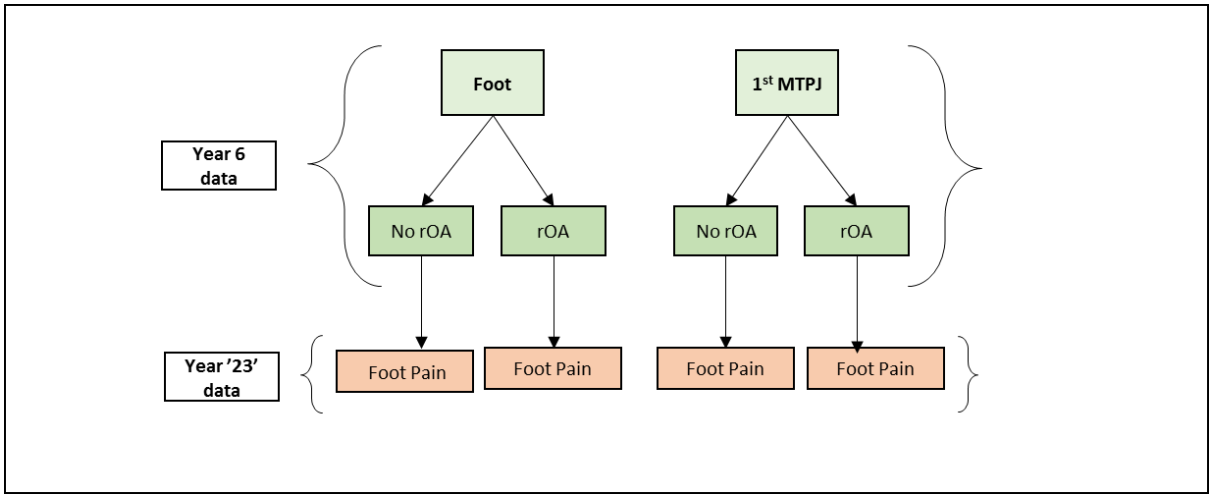


Figure 22 Natural history summarised: Prevalence of participants with and without radiographic osteoarthritis at baseline who present with foot pain at follow-up



The choice of how data were presented depended on the type of data. For instance, prevalence data specific to the foot were not dichotomised according to each foot but simply given in terms of the overall 'either foot' prevalence. This is because it is the most relevant and appropriate means in accordance with how the current body of research is presented. For the 1st metatarsophalangeal joint, both left and right feet were presented without a combined category for 'either foot' as combining feet would not have been appropriate when the 1st metatarsophalangeal joint was presented according to radiographic features. In terms of incidence, the combining of joints was not appropriate considering the methods used in preceding longitudinal studies on the hip and knee as demonstrated by figure 19 and 20.

In summary, results were presented in the following format:

Prevalence (two time-points): two cross-sectional analyses at baseline (year 6) and follow-up (year '23') including all subjects with x-rays at baseline and follow-up (with the exclusion of participants who had no x-ray at year 6 or '23' or where x-rays are unreadable or damaged).

Change (worsening, improvement and static condition of radiographic status): longitudinal data from the Chingford study analysing the change in radiographic foot osteoarthritis between year 6 and year '23'. All participants with radiographic osteoarthritis in the 1st metatarsophalangeal joint of either the left or right foot, regardless of the scoring allocated to joints. Change was defined as any increase or decrease of each score according to osteophytic change or joint space narrowing in each foot for each participant.

Incidence: a longitudinal study in participants without the presence of radiographic osteoarthritis in the foot at baseline (year 6) followed up at year '23' to assess the number of participants who went on to have radiographic osteoarthritis in the foot.

6.5. Results

The analysis focused on:

1. Description of the year 6 sample background and clinical characteristics
2. Description of the prevalence of radiographic foot osteoarthritis at year 6
3. Analysis of the change in prevalence of radiographic foot osteoarthritis from year 6 to year '23'
4. Analysis of the natural history of radiographic foot osteoarthritis relative to foot pain at year '23'

6.5.1. Response rate

846 (x-ray attendance unknown) participants attended the year 6 clinical visit and 332 participants (254 of whom attended x-ray) attended the year '23' visits. 197 participants could be paired according to the availability of foot radiographs at both year 6 and year '23', such that 57 from year 6 and an estimated 649 participants from year '23' were excluded due to their absence at the other visit.

6.5.2 Participant demographics

Participant demographics for the paired sample at year 6 and year '23' are shown below in Table 33.

Table 33 Demographic & clinical characteristics: year 6 & '23'

Demographic variable	**year 6**			**YEAR '23'**		
	Mean (SD)	Range	Total participants	Mean (SD)	Range	Total participants
Age (yrs)	56.8 (5.1)	49-70	197	75.7 (5.1)	68-90	197
Height (m)	161.2 (5.8)	146.5-183.0	190	158.0 (5.9)	144.0-177.0	192
Weight (kg)	68.0 (11.5)	44.4-110.2	190	69.7 (11.9)	39.9-107.0	192
BMI	26.2 (4.2)	16.7-45.0	190	27.9 (4.4)	17.1-42.2	192

**Study baseline work was taken from work carried out by Kirsten Leyland and does not belong to the thesis author (Leyland et al. 2012)*

Between year 6 and '23', average age increased by 18.9 years (56.8 years to 75.7 years). Average height decreased by 3.2cm with average weight and average BMI increasing by 1.7kg (68.0kg to 69.7kg) and 1.7kg/m^2 (26.2kg/m^2 to 27.9kg/m^2) respectively.

6.5.3 Prevalence of person level radiographic (polyarticular evaluated) foot osteoarthritis

Table 34 Prevalence of radiographic osteoarthritis at year 6 and of year '23' among participants who attended both x-ray visits

	Prevalence of foot rOA % (N=197)
year 6 (Baseline)	**95.4%** (n=188; N=197)
year '23' (Follow-up visit)	**82.2%** (n=162; N=197)
year 6 & '23' Difference between visits	**-13.2%** (n=16; N=197)

The prevalence of radiographic foot OA was 95.4% at year 6, and 82.2% at year '23' (Table 34) demonstrating a 13.2% reduction in the prevalence of radiographic osteoarthritis following the 17 year interval follow-up visit.

Table 35 Prevalence of change from year 6 to year '23' among paired participants

	Number of participants at baseline (year 6) used in the analysis	**Percentage and number of participants at follow-up (year '23')**
Change (rOA+ to rOA- OR rOA- to rOA+)	197	**21.3%** (42/197) Change from any status to any other status (35 go from ROA+ to ROA- and 7 from ROA- to ROA+)
No Change (Status remains the same from any possible status rOA+/rOA-)	197	**78.7 %** (155/197) Stay the same status as baseline (either ROA+ or ROA-)

Change from presence to absence of radiographic foot osteoarthritis or absence to presence of radiographic foot osteoarthritis was observed in 21.3% of participants. 78.7% had no change in foot status between year 6 and year '23' (Table 35).

6.5.4 Prevalence of joint specific radiographic foot OA at year 6 and year '23'

The prevalence of the 1st MTPJ radiographic osteoarthritis was consistently higher in year '23' compared to year 6 in both feet and in both radiographic features. The difference in prevalence of radiographic osteoarthritis within the 1st MTPJ between year 6 and year '23' ranged between 4.1% and 4.7% with the exception of the right foot osteophytic change which demonstrated a 9.8% difference in positive radiographic osteoarthritis (Table 36).

Table 36 Prevalence of year 6 and year '23' paired sample in the 1st metatarsophalangeal joint (1st MTPJ)

	Left 1st MTPJ			Right 1st MTPJ		
	Osteophytes % (N=193)	**Joint space narrowing % (N=193)**	**rOA (OP & JSN/OP or JSN)**	**Osteophytes % (N=193)**	**Joint space narrowing % (N=193)**	**rOA (OP & JSN/OP or JSN)**
year 6 Prevalence	**20.2%** (39/193)	**7.8%** (15/193)	**22.3%** (43/193)	**22.8%** (44/193)	**7.8%** (15/193)	**24.9%** (48/193)
year '23' Prevalence	**24.4%** (47/193)	**12.4%** (24/193)	**26.4%** (51/193)	**32.6%** (63/193)	**12.4%** (24/193)	**33.7%** (65/193)
year 6 & '23' Difference between visits	**+4.1%** (8/193)	**+4.7%** (9/193)	**+4.1%** (8/193)	**+9.8%** (19/193)	**+4.7%** (9/193)	**+8.8%** (17/193)

6.5.5 Natural history of radiographic 1st metatarsophalangeal joint osteoarthritis

Table 37 Natural history of 1st MTPJ radiographic osteoarthritis

	N	Left 1st MTPJ ROA	Right 1st MTPJ ROA
Change (rOA+ to rOA- OR rOA- to rOA+)	193	**15.5%** (30/193) (11 go from rOA+ to rOA- and 19 from rOA- to rOA+)	**18.1%** (35/193) (9 go from rOA+ to rOA- and 26 from rOA- to rOA+)
No Change (Status remains the same from any possible status rOA+/rOA-)	193	**84.5%** (163/193) stay the same status as baseline (either rOA+ or rOA-)	**81.9%** (158/193) stay the same status as baseline (either rOA+ or rOA-)
rOA progression (rOA- to rOA+)	150 (left)* 145 (right)*	**12.7%** (19/150) change from rOA- to rOA+	**17.9%** (26/145) change from rOA- to rOA+

The change between presence and absence with either as the outcome at follow-up was higher in the right foot by 2.6% and was higher for incidence by 5.2%. Values for change and incidence were low ranging from 19 to 35 participants for all groups. No change was considerably higher at 84.5% and 81.9% for the left and right feet respectively. Incidence was found to be low at 12.7% with a higher prevalence in the right foot of 17.9% (Table 37).

6.5.6 Changes of radiographic 1st MTPJ OA from year 6 to year '23'

To determine the extent of change, scores for change in the LFA radiographic grades were calculated (Table 38).

Table 38 changes in radiographic score for the 1st MTPJ between year 6 and year '23'.

	1st Metatarsophalangeal joint (1st MTPJ) N=193			
	Left foot		Right foot	
Grade change	OP	JSN	OP	JSN
0-0	20.7% (40)	15.5% (30)	23.3% (45)	11.9% (23)
0-1	7.3% (14)	18.7% (36)	8.3% (16)	20.2% (39)
0-2	1.6% (3)	0.5% (1)	2.1% (4)	0.5% (1)
0-3	0.5% (1)	0.5% (1)	0.5% (1)	0.0% (0)
1-0	15.5% (30)	11.9% (23)	9.8% (19)	14.0% (27)
1-1	26.9% (52)	40.4% (78)	21.8% (42)	40.0% (77)
1-2	6.7% (13)	3.1% (6)	9.3% (18)	4.1% (8)
1-3	0.5% (1)	1.6% (3)	2.1% (4)	1.6% (3)
2-0	2.1% (4)	0.0% (0)	0.0% (0)	0.0% (0)
2-1	3.1% (6)	1.0% (2)	3.6% (7)	1.6% (3)
2-2	6.7% (13)	2.1% (4)	9.8% (19)	2.1% (4)
2-3	5.2% (10)	1.0% (2)	7.3% (14)	2.1% (4)
3-0	0.0% (0)	0.0% (0)	0.5% (1)	0.0% (0)
3-1	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
3-2	0.5% (1)	0.0% (0)	0.5% (1)	1.0% (2)
3-3	2.6% (5)	3.6% (7)	1.0% (2)	1.0% (2)
	100% (193)	100% (193)	100% (193)	100% (193)

Key

Colour	Interpretation relating to change
	No change
	Positive change
	Negative change

The most notable change in individual scores from table 38 appear at the low levels for no radiographic osteoarthritis between the '0' and '1', meaning that the diagnosis of osteoarthritis in the joint did not change at year '23' for a large proportion of participants. The change in scores at

the higher levels resulting in a diagnosis of radiographic osteoarthritis was a low proportion of participants.

6.5.7 The natural history of developing symptomatic radiographic foot OA

Table 39 Prevalence of foot pain at year 6 and year '23'

N=193	Left foot	Right foot	Left or right foot
year 6 Prevalence	**11.4%** (22/193)	**7.3%** (14/193)	**15.0%** (23/193)
year '23' Prevalence	**17.1%** (33/193)	**16.5%** (32/193)	**20.7%** (40/193)

**year 6 is likely overestimated prevalence as it also includes symptoms of swelling and stiffness and additionally referred to the previous year (compared to year '23' which referred to the past month).*

Foot pain in all instances increased between year 6 and year '23' for the left, right and either foot. These increases were 5.7%, 9.2% and 5.7% respectively with the right foot having the lowest prevalence of foot pain at both years (Table 39).

Table 40 Progression of asymptomatic radiographic osteoarthritis at year 6 to symptomatic radiographic osteoarthritis at year '23'.

	rOA Left foot	rOA Right foot	rOA Left or right foot
year 6 asymptomatic	**89.2%** (148/166)	**93.0%** (160/172)	**84.4%** (152/180)
year '23' Symptomatic (Foot pain +ve)	**12.2%** (18/148)	**16.3%** (26/160)	**17.1%** (26/152)

In participants with asymptomatic rOA, at year 6, 12.2% (left foot), 16.3% (right foot) and 17.1% (either foot) were symptomatic at year '23' (Table 40).

Table 41 Natural history: Baseline foot radiographic osteoarthritis with co-existing presence of foot pain and co-existing foot pain at follow-up

	rOA Left foot	rOA Right foot	rOA Left or right foot
year 6 symptomatic Foot pain +ve	**10.8%** (18/166)	**7.0%** (12/172)	**15.6%** (28/180)
year '23' Asymptomatic Foot pain -ve	**50.0%** (9/18)	**16.7%** (2/12)	**39.3%** (11/28)

In participants with symptomatic radiographic osteoarthritis at year 6, 50.0% (left foot), 16.7% (right foot) and 39.3% (either foot) were asymptomatic at year '23' (Table 41).

Table 42 Prevalence of foot pain at (Year '23) with presence and absence of radiographic OA at year 6.

		Co-existing foot pain Yr '23'		
Anatomical location	**rOA at Yr 6**	**Left foot**	**Right**	**Either foot**
Foot*	Present	**16.6%** (28; 169)	**16.6%** (29; 175)	**27.5%** (38; 138)
	Absent	**27.3%** (6; 22)	**25.0%** (4; 16)	**37.5%** (3; 8)
1st MTPJ	Present	**15.9%** (7; 44)	**20.4%** (10; 49)	**22.7%** (15; 66)
	Absent	**18.4%** (27; 147)	**16.2%** (23; 142)	**20.8%** (26; 125)

**Polyarticular evaluated radiographic foot osteoarthritis*

Polyarticular evaluated radiographic foot osteoarthritis (27.5%) and 1st metatarsophalangeal joint (22.7%) radiographic osteoarthritis were found to be similar (Table 42) when considering presence of radiographic osteoarthritis at baseline (year 6) compared to presence of foot pain at follow-up (year '23').

6.6. Summary of results

6.6.1. Paired sample characteristics

Participants were found to have increased weight, smaller average height and a consequently higher BMI at year '23' compared with year 6.

6.6.2. Prevalence of radiographic foot OA and of foot pain at year 6

At year 6, prevalence of radiographic foot level osteoarthritis was higher than that found in year '23'. The 1st metatarsophalangeal joint in contrast to the foot (polyarticular evaluated radiographic osteoarthritis) had a higher observed prevalence of radiographic osteoarthritis in year '23' compared to year 6 when individual features of each joint were scored.

Foot pain was higher at year '23' compared to year 6 which as an important clinical finding.

6.6.3. Analysis of the change in prevalence of radiographic foot OA from year 6 to year '23'

One fifth of participants demonstrated a change of diagnosis of rOA in the feet such that 21.3% changed between presence or absence of radiographic osteoarthritis with change in either direction. In the feet, 78.7% of participants demonstrated no change of status in the diagnosis of rOA from year 6 and year '23'. Participants investigated for radiographic change in the 1st metatarsophalangeal

joint showed less change than that observed for foot level osteoarthritis (polyarticular evaluated osteoarthritis). New cases of 1st MTPJ radiographic osteoarthritis occurred in 12.7% and 17.9% in the left and right feet at year '23'. It was evident within the individual scores for those joints that subtle changes were more common and the most common change was between '1' and '0', and '0' and '1'.

6.6.4. Analysis of the natural history of developing symptomatic radiographic foot OA

Foot pain at year '23' increased where presence of asymptomatic rOA+ (without foot pain) existed at year 6. Symptomatic radiographic osteoarthritis (with foot pain) at year 6 tended to decrease among the same participants evaluated at year '23'. Small differences showed that the prevalence of follow-up foot pain was higher when radiographic osteoarthritis was present in the 1st MTPJ at year 6 compared to when 1st MTPJ radiographic OA osteoarthritis was not present.

6.7. Discussion

The results from this study provide new prospective evidence for the prevalence and natural history of radiographic foot OA in a large sample of older women from a UK population-based cohort. The analyses also provide novel data on the progression of asymptomatic and symptomatic radiographic foot OA.

From the literature review (chapter 2, section 2.6.), most current evidence for the prevalence of radiographic foot OA is attributable to cross-sectional analytical data with small sample sizes. The lack of foot specific longitudinal data have consequently been criticised as limiting the understanding of the full pathophysiology and clinical relevance of OA within the foot, which has led to an inadequate evidence base for evaluating clinical interventions (NICE 2014; Roddy et al. 2015). The most relevant work to this study is the north Staffordshire based study by Thomas et al. (2004), with the prospective set up of a study and anticipated return three years later with the intention to focus on pain and osteoarthritis variables in the foot. However, the subsequently published research appeared to relate to cross-sectional work rather than making use of any longitudinal data. No other studies are known that have used longitudinal data to consider natural history of radiographic foot osteoarthritis over seventeen years. This sets a precedent, but also results in a difficulty making comparisons between results.

To simplify the discussion the natural history of radiographic foot osteoarthritis has been structured into radiographic foot osteoarthritis, foot pain, radiographic osteoarthritis of the 1st MTPJ, and symptomatic radiographic osteoarthritis of the 1st MTPJ.

6.7.1. Background demographics at study baseline, x-ray baseline and x-ray follow-up

The age difference seems appropriate considering that the difference between year 6 and '23' was more due to the data collection dates that the officially documented (year number) 17 year difference would suggest. It is of interest that participants averaged in the 'overweight' category from year 6 to year '23' despite the observed increase among older participants at year '23'. Increased BMI is an expected outcome among older participants (Rolland-Cachera et al. 1991). However, the upper parameter of BMI at baseline reduced marginally at follow-up, although it was not investigated whether there was any association between obesity and mortality. It is also plausible that this could be attributed to the overall height decrease with age. Height was found to be 3.2cm less among year '23' participants which was a small difference, and expected and affirmed by the reporting of women's height in relation to increasing age in reference data by Samson et al. (2000).

6.7.2. Natural history

6.7.2.1. Natural history of radiographic osteoarthritis of the foot

The higher prevalence of radiographic foot osteoarthritis found in year 6 compared to year '23' (difference of 23%) was surprising. Previous epidemiological work has recognised the biological plausibility of the improvement of the condition in small numbers of sufferers with osteoarthritis in the hip and knee (Arden and Nevitt 2006) due to the pathophysiological process outlined in chapter 2 (2.1.1). In an investigation of the knee, a study using the same Chingford Women study population with a similar follow-up period of 14 years 1.7% of participants had a decrease in radiographic osteoarthritis. Considering the physiological differences and joint constructs (polyarticular evaluated in the foot), it is not surprising that this differs considerably, although this does not help clarify the context of what was found for natural history in the foot. However, it is of note that the comparison of foot radiographic osteoarthritis and other joint radiographic osteoarthritis (ie. hip or knee) involves heterogenous study designs, as radiographic osteoarthritis of the foot incorporates 5 joint variables of both feet to establish foot osteoarthritis, rather than the single joint evaluations of the hip or knee.

Of note, variation in prevalence of radiographic foot osteoarthritis due to scoring technique was highlighted in chapter 4, section 4.4.2. In addition, differences in the scoring of OPs and JSN for each joint due to the resolution of plain film radiographs as used in year 6, against high resolution

computerised images used in year '23' were discussed. In chapter 4, both factors could have produced a higher prevalence estimate for the year 6 data than that of the year '23'.

6.7.2.2. Natural history of pain in the foot

Prevalence of foot pain at year '23' was higher than at year 6. In chapter 5 (section 5.6) the cross-sectional analyses for year '23' demonstrated an increase of pain with increasing age among women aged 70-74, 75-79 and 80-84 and is therefore plausible that the younger cohort at baseline would have a lower prevalence. It should be noted, however, that overall, conclusions were difficult to establish in terms of pain patterns with age. However, it is likely that year 6 pain was overestimated considering that this variable included swelling and stiffness in addition to pain in each foot. In support of this, Roddy et al. (2011) identified onset of foot pain following three years from baseline occurred among 8.1% of patients. Although this was a detailed investigation of foot pain, it related to the case definition of disabling pain identified using the MFPDI functional section of the questionnaire.

6.7.2.3. Natural history of radiographic osteoarthritis of the 1st MTPJ

Prevalence of radiographic osteoarthritis within the 1st MTPJ was higher at year '23' than at year 6 (change was 4.1% left foot; 8.8% right foot).

The higher prevalence at year '23' was an encouraging result and demonstrated a more biologically plausible outcome than when considering radiographic foot osteoarthritis discussed above.
The definition for radiographic osteoarthritis at the 1st MTPJ used a threshold of grade '2' or more whilst a score of '1' or '0' indicated absence of radiographic osteoarthritis in the 1st MTPJ. Over time, where the score of osteoarthritis did not change, this tended to occur more frequently for the lower scores of '1' or '0'. There was less change observed over time for the higher grades of 2 or 3. This is not surprising as participants were considerably younger when the year 6 foot x-rays were performed and thus at this time more severe radiographic osteoarthritis in the 1st MTPJ would be less likely to exist.

Change in radiographic osteoarthritis at the 1st MTPJ was most evident for only one grade difference between Year '6' and year '23' which suggests that changes in radiographic osteoarthritis are small or slow among women from middle to older age. It is difficult to compare these findings directly to other work as there is no research which has considered radiographic foot osteoarthritis using longitudinal data. Therefore, the exploration of epidemiological patterns of change in radiographic

osteoarthritis of the 1st MTPJ in this chapter provides novel data, of which the need has been recognised by Roddy et al. (2018).

It is interesting that the participants exhibiting no changes from presence to absence or absence to presence of radiographic osteoarthritis was high, given the considerable time of 17 years that elapsed between baseline and follow-up x-rays. Contrary to the consideration of radiographic foot osteoarthritis, progression from no radiographic osteoarthritis in the single joint the 1st MTPJ at year 6 to presence of radiographic osteoarthritis was higher at year '23'.

The difference in the 'change' category between rOA+ (positive diagnosis of radiographic foot osteoarthritis) to rOA- (no diagnosis of radiographic foot osteoarthritis) and rOA- to rOA+ was an important one, as they did not appear to differ. This was surprising considering the biological plausibility of rOA- to rOA+ and biological implausibility of rOA+ to rOA-. However, the higher prevalence of change from rOA- to rOA+ was important in providing meaningful results within the exploratory nature of the results. It should be noted that significant differences were not tested as statistical power could not be achieved with the small sample sizes in the results. The established work on reliability provides understanding and context to these results showing a change from rOA+ to rOA-.

Chapter 4 discussed the disparity in the quality of images of year 6 and '23' that were evaluated, which resulted in greater uncertainty in the images with lower resolution and consequent overestimation of the presence of radiographic osteoarthritis. To offset the bias, all joints with uncertainty were removed from the analysis. However, there was likely to be greater uncertainty at year 6 where poorer image quality existed than at year '23', thus resulting in overestimation of presence of radiographic osteoarthritis. This is likely to have resulted in a progression being observed between year 6 and year '23' of presence to absence of radiographic osteoarthritis in the 1st metatarsophalangeal joint. This is recognised as a limitation, and given the period of assessment it would be difficult to minimise its effect on the results. The only mechanism to improve this within our study design, other than using time points where digital equipment was available, would have resulted in the study becoming a prospective study. This was not feasible given the additional financial expense required to perform such an investigation. Alternatively, analogue plain film x-rays could have been digitised to reduce some of the bias demonstrated through the quality of images at the two time points. Again, this would have required additional financial expense and was therefore not feasible. However, it is an important consideration for future longitudinal studies of the foot

involving radiographic assessment with the potential to reduce the true prevalence estimate due to better accuracy of measurements.

Having accepted that disparity between x-rays was a limitation of the study, the most important and novel result was where a change from absence of radiographic osteoarthritis in the 1st MTPJ at year 6 to presence of radiographic osteoarthritis in the 1st MTPJ at year '23' demonstrated 12.7% and 17.9% in the left and right foot respectively. As an indirect comparison, incidence of radiographic osteoarthritis in the knee was found to exist at 2.3% of a studied population over a 14 year period by Leyland et al. (2012), and Franklin et al. (2011) found 2.5% to have radiographic osteoarthritis of the hips with follow-up at 11 and 28 years after the original diagnosis.

Finally, what was surprising was the low level of onset of radiographic osteoarthritis within the 1st MTPJ over a long period of time. Considering polyarticular evaluated foot osteoarthritis was high (91.3%) there was little scope for onset due to the ceiling effect. However, the pragmatic approach of investigating the 1st metatarsophalangeal joint was important particularly due to its lower baseline prevalence of 22.3% (left foot) and 24.9% (right foot), and was a more interesting and meaningful analysis as there was greater potential for onset of radiographic osteoarthritis. Yet over a long period of 17 years where participants progressed from middle age to older age, progression to radiographic osteoarthritis was low. Year 6 incidence of foot osteoarthritis was overestimated due to the noise created by lower quality radiographic images whereas year '23' better quality images provided more accurate prevalence.

6.7.2.4. Natural history of asymptomatic radiographic osteoarthritis of 1st MTPJ at year 6 relative to presence of foot pain at year '23'

It is important to consider that the absence of foot pain was low with 8 participants in this category, meaning that caution should be taken in the interpretation of this result. The findings indicate a potential trend for radiographic osteoarthritis in the 1st metatarsophalangeal joint at year 6 being a predictor of foot pain seventeen years later. Key to the natural history in terms of participants who developed pain were the more specific single joint assessments of the 1st MTPJs whereby pain was experienced at follow-up in the same joint when participants also had presence of radiographic osteoarthritis in the joints. This was true for the right foot and for the consideration of either foot, but was not true for polyarticular evaluated joints. This provides the suggestion that asymptomatic radiographic osteoarthritis may be an early indicator of future pain and warrants further investigation with more specific reference to pain in the studied joints with radiographic osteoarthritis.

The current body of research in terms of natural history specific to prevalence of radiographic osteoarthritis is poor when considering specific reference to the feet. However, the observation that 17.1% of participants who had radiographic foot osteoarthritis developed foot pain was important. This suggests that there may be merit in providing early diagnosis and management of asymptomatic radiographic foot osteoarthritis.

6.7.3. Strengths and potential limitations

The strengths of this study include the following:

1. *Longitudinal cohort study design with follow-up*

Longitudinal cohort studies are infrequently used in research, most likely due to the expensive and time consuming nature of the design. The strength of a longitudinal study design is described by Gravetter and Forzano (2011) as the absence of cohort effects due to one group being observed with similar traits or characteristics, therefore removing bias due to covariates. Additionally, the authors explain that changes can be observed in longitudinal designs with increasing age which is recognised in this thesis as the natural history of disease. Hammond (2014) also explains that observation of the natural history of a disease can be carried out without systematically manipulating its state. Unique to this study is the large interval between data collection, which means that middle aged women could be observed and then the same participants could be observed in older age to consider the onset and progression of disease. Despite studies having investigated radiographic foot osteoarthritis, such as the CASF study, COS (Clearwater Osteoarthritis Study), Johnston County Study (Golightly 2012), Australian retirement village study (Menz et al. 2007), the Chingford 1000 Women study was the first to have the resources to enable a longitudinal design following two data collection points. This enabled prevalence of radiographic foot osteoarthritis to be observed in middle aged and older aged women, due to the recruitment of participants with similar background demographics. It also enabled the investigation of onset and progression of radiographic foot osteoarthritis whilst also having foot pain data to understand the clinical relevance.

2. *Large sample size with a large response rate at follow-up*

The sample consisted of 332 participants assessed at year '23' during the clinical visit and 223 participants who were assessed radiographically. This is similar to the 197 radiographically assessed by Menz et al. (2009). It is well established that a small sample size will result in inadequate statistical power and consequently affect the meaning of results. Unique to this study is the large

sample size within a longitudinal design investigating radiographic foot osteoarthritis. This not only means that the correct power was established for meaningful results, and being able to effectively define onset and progression. At baseline of the Chingford 1000 Women study, 1003 participants attended with 332 in attendance at year '23' which is 33.1% from Year 0 and 64.3% from the previous follow-up at Year 20 (N=516). Notably, participants completed all or the majority of clinical assessments with the exception of the radiographic imaging at year '23' (N=254). The response rate for those in attendance for radiographic imaging at year '23' from baseline Year 0 (N=970) was 26.2% and based on the previous clinical assessments at Year 20 (N= 497) was a response rate of 51.1%. The good response rate was likely in part to do with the sense of belonging through long term involvement in a study as identified by Pearson (2011) but may have also been attributable to the consistency of patient contact with the research assistant (MD) who was involved in the study from a very early point through to and inclusive of year '23'. In a study by Baruch (1999) investigating the response rate within 175 studies, the response rate was found to be an average of 55.6% (SD 19.7). For this thesis investigation, Year 20 to '23' response rate was above the average defined by Baruch (1999) and the x-ray response rate was just below.

3. *Population study representative of a general population of older women in the UK*

Study 3 is a unique addition to the body of research in that participants were recruited at baseline for the study in 1989 on the basis of any presence or absence of pathology. Although the focus of research was initially to investigate osteoporosis and latterly osteoarthritis, there was no assignment of participants as part of the inclusion or exclusion criteria at baseline. The population characteristics at baseline were comparable to women of the general population in weight, height, BMI and socio-economic profile (Arden et al. 1996). The research has therefore filled a gap in the literature and met the requirement for a study population more representative of the general population for epidemiological investigation of radiographic foot osteoarthritis in the foot.

The use of a cohort representative of the general population is an important inclusion within the research presented in this thesis. The key research papers presenting radiographic osteoarthritis using the more sensitive and validated approach of the LFA used an Australian population recruited from a retirement village (Menz et al. 2007) and a population recruited with symptoms of pain in the feet (Roddy et al. 2015).

4. *Extensive novel data defining the natural history of radiographic foot osteoarthritis and foot pain*

Through this study the natural history of radiographic osteoarthritis in the foot with focus on the 1st MTPJ has been comprehensively explored. The research is the first to describe the natural history of radiographic foot osteoarthritis over such a long time period. In this study, data are presented on individual 1st MTPJ prevalence at year 6 and year '23' according to the assigned scoring of the 1st MTPJ changes. In addition the natural history of foot pain was also explored for the same time period. The study data were an important contribution to research in showing that symptomatic radiographic osteoarthritis increases from middle age to older age and that a high proportion of participants with symptomatic radiographic osteoarthritis continue to experience pain seventeen years later.

The data from this study have a vital role in understanding the nature of temporal changes in radiographic foot osteoarthritis. This is not only a benefit in understanding the presentation among women in a general population to assist with clinician diagnostic skills, but equips clinicians with the knowledge of how to focus treatments and management plans. In terms of research, there is a greater understanding of target populations that should be considered and studied in the future.

Potential limitations that should be considered revolve mostly around the use of differing methods that exist between the two time points in the radiographic imaging scoring techniques. These are considered as follows:

1. *Case definition of foot osteoarthritis for longitudinal analysis.*

As can be seen in figures 20, 21 and 22, there is a disparity between the diagnosis of radiographic foot osteoarthritis and radiographic knee (or hip) osteoarthritis. The problem presented relates to the additional number of conditional variables that constitute a definition of radiographic foot OA. Where the knee is dependent on one joint having presence of either radiographic feature (osteophytic or joint space narrowing) in one radiographic projection, the foot requires a definition for the presence of either radiographic feature in any one of five joints in one of two projections. The approach to defining radiographic foot osteoarthritis according to Menz et al. (2007) could therefore be considered as a multifaceted and multidimensional approach (or dual radiographic projections) when compared to the standardised methods observed in diagnosing hip or knee osteoarthritis which rely solely on the presence of radiographic change in a single joint with a single radiographic projection (Kellgren and Lawrence 1963; Ingvarsson et al. 2000).

Therefore, there was the need to focus on one joint in a single projection. When considering the most appropriate joint to investigate, the number of ungradable joints determined within the chapter 4 investigation were considered. The 1st metatarsophalangeal joint was found to be the joint that was the most reliable to score using the atlas. The lower frequency of ungradable joints indicates less uncertainty in evaluating joints, which would suggest that these results are closer to the true value of prevalence. This compares to joints where greater uncertainty is observed which may demonstrate a bias towards higher frequency of joints with radiographic osteoarthritis, resulting in an over-estimation. To address this uncertainty in future work, there should be a focus on minimising the observer uncertainty, and thus improving accuracy when using the LFA. Indeed, the effect of joints considered 'ungradable' being graded as a higher score was discussed previously in chapter 4 and the direct impact is outlined in Appendix 16.

2. *Techniques whilst using the LFA*

Prevalence was established using the traditional method with the LFA (technique 1) which was identified in chapter 4 as the most reliable technique for cross-sectional prevalence. Additionally, the prevalence for radiographic foot osteoarthritis was presented for the technique which excluded 'ungradable' joints as the importance of this method was established in the presentation of results using a longitudinal study design. The traditional technique established a higher prevalence than the excluded 'ungradable' joints technique, and a higher prevalence was established for both techniques at the year '23' return visit.

Prevalence was found to be high in the paired sample for year 6 and year '23' visits, as was anticipated following the completed work in chapter 5 which demonstrated high prevalence of radiographic foot osteoarthritis in the year '23' cross-sectional analyses (91.3%). It was not anticipated that a higher prevalence would be established in the year '23' (return visit) data. Of relevance is work which was carried out for the upgrade thesis for the award of 'Master of Philosophy' which identified a year '23' (N=51) prevalence of 92.2%, similar to that reproduced for this thesis. The year 6 (N=93) data established a prevalence of 98.9% for radiographic osteoarthritis and in both years the same methods were replicated between the theses. Although the suggestion was made that these results were indicative of the experience gained over time, whereby year 6 (former radiographic evaluations) were carried out by the thesis author (PMc) with less experience than the (latter) year '23' assessments, more detailed investigation of the feasibility of using the LFA on the Chingford 1000 Women study has affirmed the original results with a higher baseline prevalence and has demonstrated other reasons for this. It is noted however, that the findings and

discussion in chapter 4 are in no way invalidated, as the year 6 prevalence was 3.5% lower when re-evaluated using the same methods for the purposes of this thesis. This compares to the 9.1% difference observed between the full year '23' cohort described in chapter 5 (91.3%) and chapter 6 (82.2%) established prevalence. A direct descriptive comparison cannot be made with the prevalence established for this chapter as it excludes the lateral projection. Although there is a difference in prevalence, it is possible that a 'learning effect' affected the prevalence of the results in the initial chapter 4 work.

3. *Technological advances in equipment between baseline and follow-up*

This can be explained through several factors that account for an apparent decrease in the prevalence of radiographic foot osteoarthritis. Limitations existed in the methods used for the year 6 and year '23' visit x-raying techniques. One limitation was the format on which x-rays were recorded. In year 6 (1995), x-rays were recorded using polymer film sheets compared to x-rays for year '23' (2014-15) which were recorded on a digital system using image viewing software programmes for radiography. This presents a number of limitations in itself as no contrast medium is available for the year 6 x-rays, where contrast adjustment is available in year '23' x-rays. It is possible that this could be eliminated as a limitation in the future by digitising polymer radiographic imaging to view on image viewing software, whereby the contrast can be adjusted.

Further to this, the technology and equipment for radiographic imaging has inevitably improved over the 17 year period, particularly with the introduction of digital equipment and computer software. This therefore brings into question the disparity that may exist as a consequence in the detail that can be physically observed when evaluating joints for radiographic signs of changes. Tables 20 to 22 theorise the impact of the disparity of image quality observable on x-ray at year 6 and '23' on the prevalence. This disparity is quantified according to the joints identified as 'ungradable'. It is clear that this contributed to the greater uncertainty in year 6 radiographic images whilst using the LFA.

4. *Use of female participants only*

An obvious limitation is the use of women only in this study meaning the results of the study are only generalizable to women, and men have not been tested to establish if any differences exist compared to women.

5. *Construct of the LFA compared to the Kellgren and Lawrence atlas*

The limited research available on patterns of change would be difficult to bring into the discussion with regards to dispersion or prevalence of radiographic osteoarthritis. This is on the basis that the LFA construct which consists of a four grade system of identifying radiographic osteoarthritis differs from the more conventional five grade system pioneered by Kellgren and Lawrence (1958). With the increased atlas scores in the Kellgren and Lawrence atlas, the sensitivity will likely be higher because there are more measures by which to interpret data (Bowling 2009).

6.8. Conclusion

The findings of this investigation provide new evidence that radiographic foot OA does change over time, becoming progressively worse. The findings also indicate that individuals who have radiographic foot OA and no symptoms are likely to progress over time to have foot pain. Trends in the study data indicate that participants who have asymptomatic radiographic osteoarthritis should not be clinically ignored in respect of subsequent pain that may ensue in the future. As this study was limited to descriptive data, future research should focus on exploring the associations of radiographic foot osteoarthritis and co-existing foot pain further.

6.8.1. Key Points

Natural history of rOA and foot pain

Key points

- 78.7% of participants remained static in diagnosis of foot OA over a 17 year follow-up where 21.3% changed in rOA diagnosis.
- Polyarticular evaluated rOA is not an appropriate consideration for onset and progression of rOA of the foot and should relate to single joints.
- Onset of the 1st MTPJ rOA in the left (12.7%)and right (17.9%) foot after 17 years provides novel data.
- Foot pain over 17 years increased from presence of asymptomatic rOA in the foot.

6.8.2. Summary

Natural history of radiographic foot osteoarthritis and foot pain were presented using baseline with seventeen year follow-up data to define novel epidemiological data in relation to the foot. A particular focus on the natural history within the 1st metatarsophalangeal joint was presented, creating a precedent for study design for other joints whilst also identifying the need to target patients who do not have pain at baseline and may progress to developing pain when radiographic osteoarthritis is present from baseline. These key contributions to research and implications of the thesis work (including study 1 and 2) will

be further explored in the final chapter, whilst also outlining the consequent direction of future research.

Chapter 7 Discussion

7.0. Introductory chapter summary

This chapter concludes the work of the thesis, reviewing key themes and results from the three thesis studies whilst also critiquing methods and considering strengths and weakness of the work. Definitions of radiographic foot osteoarthritis and foot pain are discussed with relation to global consensus. Finally, the suggested direction for future research and implications for future clinical practice are discussed and concluded.

7.1. Introduction

The primary aim of this thesis was to determine the natural history of radiographic foot osteoarthritis and co-existing foot pain among older aged women taken from a population-based cohort within the UK. It was anticipated that the data generated would determine an estimated prevalence of painful radiographic foot osteoarthritis among the UK population of older women and enable the clinical importance of foot pain to be determined following an earlier diagnosis of radiographic foot osteoarthritis.

The three study chapters four, five and six were driven by the need to produce robust results demonstrating consistent reliability and validity, with a theme of feasibility featuring in all three chapters. The chapters concluded with discussion of prevalence in radiographic foot osteoarthritis and foot pain comparable to the current body of research, and novel results in longitudinal analyses demonstrating the natural history presenting among women.

Study 1 (chapter 4) explored the reliability, validity and appropriateness of the MPhil student using the Australian based foot atlas (LFA) on a UK population-based cohort of older women recruited from the general population. Study 2 (chapter 5) investigated the prevalence of radiographic osteoarthritis in the foot, foot pain and co-existing radiographic osteoarthritis and foot pain. Study 3 (chapter 6) investigated the prevalence and natural history of radiographic foot osteoarthritis and foot pain. These chapters have fulfilled the aims set out in the method of the thesis and the learning outcomes identified within the Doctor of Philosophy programme. These studies have contributed to the knowledge and understanding of radiographic foot osteoarthritis and foot pain research by generating novel and unique data on the co-existence and natural history of radiographic osteoarthritis and pain in the feet and 1st MTPJ respectively within a UK population-based cohort of older women.

These studies have incorporated a breadth of research knowledge into their conception, design and methodology to meet the need of knowledge inadequacies in rheumatological and podiatric research. Key to this thesis is the fulfilment of a research need in the co-existence of radiographic osteoarthritis and pain in the feet, and the natural history of radiographic foot osteoarthritis.
The challenge of differing data collection techniques used in the longitudinal type data required a revised approach to standardised methods of analysis for cross-sectional work. These issues were identified and resolved by the MPhil student and incorporated into the thesis following agreement with the supervisory team. The research produced has adhered closely to epidemiological principles and has advanced the current body of research beyond what has previously been presented in the literature, with detailed analysis of the literature to identify the gap in knowledge.

7.2. Radiographic scoring technique for foot osteoarthritis

The LFA conceived by Menz et al. (2007) was the first atlas to consider radiographic osteoarthritis with anatomical specificity in the feet following the work by Kellgren and Lawrence (1958) which pioneered the evaluation of radiographic osteoarthritis in other key joints. The LFA atlas by Menz et al. (2007) is the only atlas of its kind and has provided an important and necessary contribution in the diagnosis of structural foot osteoarthritis, for research and clinical practice. The atlas demonstrates osteoarthritis across five joints, considered by the authors as the most clinically important using two projections to improve the sensitivity to pathology. Through the work of this thesis, it has been established that there is not only scope for this diagnostic method in clinical practice but also the professional freedom for podiatrists to extend their scope and incorporate this into practice.

The inclusion of five joints to establish a diagnosis of radiographic foot osteoarthritis is an interesting discussion in itself. The thesis design (involving the investigation of longitudinal data in the development of osteoarthritis) has identified the single most appropriate measure of radiographic osteoarthritis as joint level investigation rather than person-level, in accordance with longitudinal design methods of existing research studies on the hip and knee. In describing ‘radiographic foot osteoarthritis’, it is perhaps more appropriate to define this as ‘polyarticular evaluated radiographic foot osteoarthritis’. It should be considered that defining the ‘polyarticular evaluated radiographic foot osteoarthritis’ within populations is important and there is no detraction from the value of preceding research established prior to this thesis. However, when using longitudinal data, it is clear that the more appropriate method is through the consideration of individual joints, consistent with the methods within the current body of research for other joints such as the hip and knee. This is

also relevant to studies where longitudinal data collection involves both the use of analogue plain film and fully digital x-rays.

Previous research studies have made use of the Kellgren and Lawrence atlas and the LFA primarily. Where the radiographic projections were specified, the anteroposterior view was primarily used in research prior to the LFA but was often limited to using the Kellgren and Lawrence atlas and when investigating metatarsophalangeal joints (presented in tabulated work by Trivedi et al. 2010). Of note is the additional projection used within the LFA. In many respects, this is a legitimate inclusion to the atlas, as collaborative work with the radiography department healthcare professionals and managers established that there was no specific focal point for the x-ray beam which can, on occasion, affect the quality of the imaging of individual joints. The additional view may be beneficial in reducing uncertainty in evaluating the x-rays.

However, it was evident from work in chapter 5 that the additional view increased the sensitivity to the presence of radiographic osteoarthritis. This method also differed from research on the hip and knee when considering prevalence or incidence using cross-sectional and longitudinal data. Overall, the LFA should be the preferred method of radiographic classification of foot osteoarthritis. It is perhaps more beneficial to consider joints individually both in research and in clinical practice. However, in both instances, the most pragmatic approach is to maintain the consistency the LFA presents. This will not only help researchers and clinicians in the use and uptake of the atlas but also enable the investigation of other joints without the further exposure to diagnostic radiation which is in the best interests of patients and participants alike.

7.3. The prevalence of radiographic foot osteoarthritis and co-existing foot pain

Polyarticular evaluated radiographic foot osteoarthritis was found to be high among women with around nine in ten demonstrating radiographic osteoarthritis in one of five joints in either foot. This was demonstrated to be the case for the Australian population from which the LFA was derived. On a joint level this varied, with ranges between 28.4% and 78.9%. The important prevalence ranking of joints from highest to lowest (1st CMJ, 1st MTPJ, N1stCJ and the TNJ) was also of importance and externally verified by the similar pattern found in the Australian cohort. Foot pain was presented in various formats, which was established through literature review. The definition considered with the best accuracy was where participants had shaded foot pain on a foot manikin. This foot pain definition taken from the Manchester Foot Pain and Disability Index has been well established in the literature and foot manikins have been consistently used within the literature. The prevalence of foot pain among the Chingford women was 20.5% for pain experienced during more than one day in

the past month. Surprisingly only 30.0% identified having ever had pain and despite being subject to memory bias this is lower than would have been expected. However, no research is known to be able to provide comparison on pain having ever been experienced for more than one day in the lifetime of participants, and so this is a unique contribution to research in foot pain. Worth mentioning also was the inclusion of clinician diagnosed foot pain, the prevalence of which was surprisingly low and which has remained unreported in the literature until the presentation of results in this thesis.

Painful radiographic osteoarthritis was an important prevalence to present, and was found to be similar to foot pain with or without the presence of pain symptoms, at 27.5% therefore showing that one in four participants experience painful foot osteoarthritis (identified by shaded foot manikins). The more stringent definitions of disabling foot pain (the method used for identifying a definition for DFP by Menz and Morris 2005) with co-existing radiographic foot osteoarthritis was found to be almost half the prevalence of foot pain, at 11.0% and 11.6% with different definitions. This was fitting with the current albeit limited body of research of co-existing radiographic foot osteoarthritis and foot pain. However, the presentation of various pain measures played an important role in demonstrating what is currently used in the literature and how they differ by as much as a 100% difference in prevalence. From this we can ascertain that a global definition needs to be established in research particularly for foot pain where heterogeneity of research methods is particularly prevalent in an area which is already particularly complex to understand.

7.4. The natural history of radiographic foot osteoarthritis and co-existing foot pain

The natural history provided helpful prevalence on radiographic osteoarthritis at two time points among the Chingford women which were 17 years apart, from middle age to older age. On a polyarticular evaluated level (radiographic foot osteoarthritis), prevalence of radiographic osteoarthritis was higher at baseline than follow-up by 13.2%. This was unsurprising in many respects as radiographic osteoarthritis was already high (91.3%) and the inclusion of five joints to diagnose radiographic foot osteoarthritis was dissimilar from methods used for studies with longitudinal hip or knee radiographic data.

Prevalence was more appropriate and biologically plausible when considered on a joint level with the selected 1st metatarsophalangeal joints, demonstrating higher prevalence at follow-up compared to baseline in the left (4.1%) and right feet (8.8%). The prevalence change was low but indicated an important change, enabling the more detailed consideration of natural history, namely incidence. Incidence work verified the increased number of cases with radiographic osteoarthritis of the 1st

metatarsophalangeal joint that was suggested by prevalence. Incidence in the left foot (12.7%) and right foot (17.9%) was an important discovery as this is the first known description of incidence of radiographic osteoarthritis in a foot joint, and was identified as being low considering the long period of seventeen years between baseline and follow-up. The 1st metatarsophalangeal joint was of particular relevance as it demonstrated the highest prevalence of foot joint pain and has been identified as a joint in need of further research (Wilder et al. 2005).

When individual changes were presented within the 1st metatarsophalangeal joints, it was noted that greater changes were less frequent, and in many cases non-existent among participants. Where changes were seen with an apparent improvement in radiographic joint condition, the most frequent change among joints was from '1' to '0'. This did not affect the presence of radiographic osteoarthritis as scorings of '0' and '1' were considered as absence of radiographic osteoarthritis. These changes, which were not expected, were attributed to the disparity between analogue and digital methods used at baseline and follow-up respectively. The greatest prevalence of radiographic osteoarthritis demonstrating progression to worse joint condition was from '0' to '1'. Once again this did not affect the presence of radiographic osteoarthritis in joints.

When co-existing radiographic foot osteoarthritis and foot pain at baseline and foot pain at follow-up were evaluated and compared with co-existing radiographic osteoarthritis and no presence of foot pain with foot pain at follow-up, the former demonstrated a higher presence of foot pain at follow-up. This suggests that early onset of foot pain is an indicator of future presence of foot pain with the co-existence of radiographic foot osteoarthritis. The low number of participants with co-existing foot pain and foot osteoarthritis at follow-up (baseline presence of radiographic foot osteoarthritis) highlights the need to investigate this concept in the UK population with a larger sample in the future. This is one of the most important findings of the thesis as it provides clear direction for future research with the knowledge required for clinicians to consider preventative approaches for pain in their treatment plans for patients with radiographic foot osteoarthritis.

7.5. Critique of research methodologies

7.5.1. Acknowledged limitations

Only women were investigated within the thesis studies. The Chingford 1000 Women study was a unique opportunity to use an established cohort listed by the National Institute of Health as being 'an important epidemiological resource' (Richards et al. 2008). The study also gave the opportunity to consider more advanced epidemiological concepts in foot osteoarthritis and foot pain that had

never been considered in previous research studies. However, in investigating the cohort, it was limited by the inclusion criteria at inception of the study design, such that men were not recruited to the study. Work carried out in chapter 5 demonstrated important comparisons with other studies that had stratified gender and results from female participants, and which were comparable to prevalence estimates in the thesis. This limitation is a particularly important consideration for the final study chapter which was focused on novel data in the natural history of foot osteoarthritis and co-existing foot pain. Being novel data, this was the first research study relating to the foot with no prior comparable longitudinal data, even considering data comparable to a women-only participant sample. This indicates the requirement for future work on foot osteoarthritis and foot pain to consider natural history among men to characterise foot osteoarthritis in men and determine if differences exist.

Different data collection methods for x-ray between study baseline and follow-up existed on two accounts; the radiographic projections included and the technology used to capture and store radiographic images. Lateral projection at year '23' was collected in addition to the single dorsoplantar projection collected at year 6. As the LFA was developed and validated for use with both lateral and dorsoplantar projections, the most appropriate response is to use the atlas accordingly. However, another accepted limitation of using the Chingford 1000 Women study is in applying modern developments in research to an older study design and methodology. However, this limitation is minor in respect of the work carried out in the reliability chapter (4) which identified the more appropriate and therefore preferable dorsoplantar projection where availability exists of only one projection.

The intra-rater reliability testing of the atlas user was established at the beginning of the thesis work and provides a foundation for the later work in chapters 5 and 6. The start of this study was likely to have been the least reliable point of testing as this was at the start of the investigator's (PMc) work on evaluating radiographic images using the LFA, and it was therefore an effective reference point within the project. It should however be noted, that the reproducibility (intra-rater reliability) was lower than in comparable studies. This is likely due to a number of reasons, firstly, the interpretation of how joints were analysed for reliability was slightly different to the key publicised research in this area (Menz et al. 2007). Menz et al. (2007) considered reliability with the combined osteophytic change and joint space narrowing whereas in this thesis reliability considered the two features separately. Likely effects on the reproducibility of the thesis data also include having only one radiographic projection available, the semi-weight bearing nature of the x-ray procedure and plain

film images compared to the higher definition images. Finally, the fact that in the work of Menz et al. (2007) the same authors who selected the radiographic images to be used in each classification grade for the LFA were the authors on which the reliability was calculated. This introduced a possible memory bias which could have influenced better reproducibility whilst using the LFA (Menz et al. 2007). This may provide more stable predictions of reliability scores, but may not be as readily applicable to new observers using the LFA who are external to the original development team.

Limited foot pain data were available at the study baseline for corresponding foot joints or regions evaluated for radiographic osteoarthritis. Foot pain data were limited at year 6 to identifying participant pain in the left foot, right foot, or both feet. Again, this is a limitation of using a retrospectively designed prospective study and provides more detailed direction for future epidemiological work. Year '23' data used MFPDI diagrams to collect pain variables within location-specific sites of the feet. The template that was used, however, (Tables 13 and 14), may be an area in need of reconsideration when considering joint specific pain. It was originally intended that location-specific pain could be considered as part of the natural history of radiographic foot osteoarthritis. However, as the margins of the defined pain locations fall exactly on the anatomical sites of the joint margins, it is difficult to apply this template to a foot pain model that considers areas of joint pain. This gives another important indication as to the how future research can be better directed through considering the natural history of radiographic foot osteoarthritis with corresponding location-specific foot pain with the development of a more appropriate and validated template.

In the final study considering the natural history of radiographic foot osteoarthritis and co-existing foot pain (specifically incidence and progression), there was a small sample of participants to analyse in the painful foot osteoarthritis groups at baseline (Table 42; N=12-28). This was because it was not feasible within the timescale and funding parameters associated with the MPhil project. There was no preceding research which had been carried out specific to the foot. Study 3 therefore considered a novel epidemiological approach within the foot. The inability to establish power in the sample observed means that study findings should be interpreted with caution. The exploratory nature of this study has provided a good foundation for future epidemiological research on foot osteoarthritis and co-existing foot pain with the opportunity for more accurate power calculations.

7.5.2. Strengths of the study

Pain was assessed using the validated MFPDI questionnaire and foot manikins, closed and single sentence questions, patient-reported foot pain using a global pain manikin (GFP), patient-reported foot specific pain (GenFP) and clinician assessed foot pain. To capture the different types of assessment of pain, four approaches were used. These included 'Generalised foot pain', 'Global foot pain', 'Foot joint pain' and 'Disabling foot pain'. Disabling foot pain was captured in a sample of older women from the UK population for the first time.

There are five recognised areas that potentially affect the quantity and quality of conclusive data on radiographic and symptomatic foot osteoarthritis (Trivedi et al. 2010). The research generated from this study contributed towards addressing these issues with preceding research enabling the comparison of findings with the wider body of research. These areas include the variation of study populations, the radiographic projections used, the investigated foot joints, the grading system used to interpret radiographic images and the definitions used to identify radiographic foot osteoarthritis. The thesis studies used a study population representative of the general population in the UK without predefined characteristics or variables other than age and geographical region (Hart et al. 1999), although the population was specific to women. This is in accordance with epidemiological principles in establishing a prospective study and has therefore provided an important strength in the contribution to radiographic foot osteoarthritis data.

The investigation of variation of technique between radiographic projections also provided important information not only regarding the difference of prevalence between projections and the bias of results but also the reduced sensitivity to osteoarthritis using only one projection. This has helped in affirming the use of two radiographic projections in the foot to investigate osteoarthritis in line with hip and knee osteoarthritis research (Leyland et al. 2012; Franklin et al. 2011) but also identified the 'gold standard' projection where it is possible to carry out data collection or analysis on only one projection. Finally, the inclusion of the three techniques of interpretation have also contributed towards improving the variation and lack of conclusive data by exploring potential bias of results due to the grading system used to interpret radiographic images. The results of this study have therefore provided a 'gold standard' in the interpretation of radiographic images whilst using the LFA.

Longitudinal data demonstrating the natural history of radiographic osteoarthritis in the foot were presented for the first time. The opportunity to investigate natural history within the feet relating to radiographic osteoarthritis and foot pain was the first known reporting in rheumatological research. Through this work it was established that a focus on specific joints for the prevalence of radiographic

osteoarthritis was more beneficial than the consideration of the foot as a whole when considering prevalence of change and incidence. The need for standardised definitions has also been identified, in particular, the inclusion of longitudinal data should be considered at conception of a prospective study. Study 3 investigating the natural history of radiographic foot osteoarthritis and the natural history when co-existing with foot pain was a critical development of this epidemiological research. This research provides the foundation for more targeted investigation of these areas of natural history with recruitment being more specific to the selection of relevant participants, for example recruiting participants with foot pain and no presence of radiographic foot osteoarthritis with follow up to establish participants with painful foot osteoarthritis at follow-up. This research therefore fits well into the existing body of research as the key published research by Roddy et al. (2013) recruited and investigated participants with radiographic foot osteoarthritis from participants recruited with self-reported foot pain.

The thesis study differed not only in approach but also in the interpretation as participants were all women and had been recruited from a general population with no known pathology (no pathologically based inclusion criteria) or symptoms at baseline in general and within the feet. Although the work of the three studies for this thesis were developed following the work of Roddy et al. (2013), the thesis naturally slots into the body of research and fills a gap by providing the foundational epidemiology of both painful and non-painful radiographic osteoarthritis. Further to this, the semi-quantitative means of evaluating osteoarthritis using an ordinal scoring method with the LFA may cause variations in scoring technique due to its subjective nature. However, the more objective and advanced quantitative measures such as joint space width measurements used in hip and knee osteoarthritis have not been developed within the foot, most likely due to the complexities of assessing radiographic osteoarthritis in a multifaceted region of the body. Finally, it is accepted that semi-quantitative methods in diagnostic imaging uses a ‘best-fit’ model whereby one characteristic can influence another (in the case of radiographic imaging; osteophytes and joint space narrowing). Importantly, the osteophytes and joint space narrowing are not presented as separate entities but combined in each image (Guermazi et al. 2013).

A theme has been established through the work of this thesis and a considerable amount of work has been carried out to account for the lack of consensus on definition, and to cover the key definitions and variations in technique towards interpretation of radiographic foot osteoarthritis and foot pain that may influence or bias results. In chapters 4 and 5 prevalence of radiographic foot osteoarthritis, foot pain and the prevalence of disabling foot pain were found to vary depending on the definition or interpretation. This therefore represents a need to move forward with a specific

technique in grading radiographic osteoarthritis and to be clear on the definition of foot pain and of disabling foot pain. This will enable progression of future research and interventional studies, and will reduce the heterogeneity that currently exists between studies as a result of the lack of consensus. This thesis supports the use of the LFA in facilitating standardised evaluations of foot osteoarthritis whilst acknowledging the technical difficulty which can impact on the prevalence results. In addition to this, the studies have supported the use of historical radiographical images in established large population cohorts.

7.5.3. Participant samples

Participants were recruited in 1989 and demonstrated study characteristics that were representative of the population at the time, significant changes have occurred in the 27 years following the initial recruitment. Most notably, the most important cause of changes in the population have been due to the expansion of London borders into Chingford which was formerly considered to be part of Essex County. The result of this has been increased migration into and out of the area both on a local, national and international level. Although Chingford may have changed in terms of demographics for educational attainment, professional level, the population characteristics should be considered when generalising to a London based population.

7.5.4. Radiographic imaging technique

The radiographic imaging was captured using analogue x-ray equipment at year 6 in 1995 and recorded using polymer films. Year '23' (2014 to 2015) imaging was captured using digital equipment and recorded using digital software programmes. The more accurate of these data collection methods was shown to be the digital method at year '23' as this demonstrated the lower number of joints considered to be ungradable. Although it is expected that more advanced equipment would produce more accurate results, it was beneficial to support this information within foot related research. The evaluation or diagnosis of radiographic foot osteoarthritis is most commonly stated within the literature as either the Kellgren and Lawrence atlas or the LFA. The LFA has been validated and tested for reliability in Australian populations and has been tested for this thesis to establish reliability within a London or UK based sample of the general population of older women (in Chingford).

It is fair to say that the LFA is the most valid and reliable atlas for investigating radiographic osteoarthritis in the foot. The relevance as a means of investigating 'foot' osteoarthritis should however be considered with caution. In identifying radiographic osteoarthritis of the foot, it is important to consider that this is a polyarticular evaluation of five joints conditional on the presence

of only one joint having radiographic osteoarthritis in either view of either foot. This is highly sensitive and has therefore established a high prevalence of radiographic osteoarthritis. This level of 'person' radiographic foot osteoarthritis is still of importance but must be presented in an appropriate manner.

The choice of five joints is an interesting one. Menz et al. (2007) described the selection method of the five joints being based upon the premise that these were the joints most commonly affected by radiographic osteoarthritis. Although the body of evidence prior to 2007 would suggest this conclusion may be difficult to establish, it is reasonable to say that a pragmatic approach is necessary considering that the evaluation of all 32 joints in the foot would be time consuming within a clinical setting. Additionally, considering the high prevalence of radiographic osteoarthritis when considering any one of five joints, it is likely that the inclusion of more joints would further increase sensitivity to the presence of radiographic osteoarthritis and so provide meaningless results. In turn, this also brings into question the qualification for the joints that have been selected within the atlas as a means of identifying radiographic 'foot' osteoarthritis.

Finally, when considering radiographic osteoarthritis within a specific joint, the talonavicular should be considered with caution. While the 1st MTPJ, 1st CMJ, 2nd CMJ and N1stCJ radiographic osteoarthritic features are considered using the dorsoplantar and lateral projections, for the TNJ osteophytes are considered using only the lateral projection and not within the dorsoplantar projection. This could be considered an inconsistency when compared with other joints in terms of prevalence. It was noted that the TNJ consistently demonstrated the lowest prevalence within the Chingford study (chapter 5) and this was no different for other studies (North West Adelaide study and CASF study). Therefore, the interpretation of the rank of prevalence should be considered with care.

7.5.5. Radiographic evaluation of osteoarthritis

This thesis has identified definitions of radiographic foot osteoarthritis and foot pain with clarity and this in itself should be considered a strength of the thesis. Foot pain in particular has been described within the literature using often indirect definitions or referring to varying degrees to the definitions of other research studies. As a result it is difficult to ascertain with clarity how foot pain has been captured, and has been revealed by detailed scrutiny of research literature. As foot osteoarthritis is somewhat in its infancy in terms of previous and ongoing research, there has been relatively less divergence, as only two atlases have been available for diagnosis in this area, the Kellgren and Lawrence atlas and the LFA. However, even at this level, Trivedi et al. (2010) discuss the

heterogeneity of research studies whereby the specific joints that have been assessed are not described in the methods of research articles. As a result, the work by Menz et al. (2007) should be recognised as an important contribution to the field, as foot osteoarthritis was effectively identified for the first time. The atlas has been recognised as having some areas which could benefit development and exploration through future research. It may be beneficial to consider the expansion of the atlas to include more joints to provide a more comprehensive atlas of radiographic foot osteoarthritis. This will not only improve the diagnosis of radiographic osteoarthritis in clinical practice, allowing clinicians to compare the atlas to specific joints, but it will also enable the comprehensive overview of radiographic osteoarthritis in the entire foot. This would enable the thorough investigation of the joints most frequently affected by radiographic osteoarthritis for all joints, rather than through selection on the basis of anecdotal information. Future research should also consider the osteophytic change of the talonavicular joint in the dorsoplantar projections to provide prevalence comparisons and demonstrate prevalence with and without this radiographic feature in this projection.

7.5.6. Definition of foot pain

It has been established in the work of this thesis that pain was defined in a number of ways through differing outcome variables and how they were interpreted. This has presented heterogeneity within the literature on foot pain. The benefit of the work generated for this thesis was in the number of definitions of foot pain considered among the participants of one study. This provides context between foot pain variables and is a good indicator of the relative prevalence using different definitions.

The key definition that was used in more detailed analysis was where participants had identified pain by shading the relevant locations on a foot manikin. The diagram was appropriate for more detailed investigation as it was the most directive measure of capturing self-reported foot pain, rather than a generalised non-directive question. The specificity of the location of pain enabled participants to consider specific references to their experience of foot pain, meaning the overestimation of the area of pain for each participant would have been less likely. This would have been particularly relevant to participants who had a higher number of painful regions around the body. Clinician diagnosed foot pain was surprising when evaluated as it is frequently included in clinical podiatric assessments yet demonstrated low prevalence among participants. This was an important inclusion for presented foot pain prevalence as it demonstrated that foot pain identified through self-reporting is not captured to the same extent through passive joint motion by way of clinician diagnosed pain.

Disabling foot pain was an important inclusion within the thesis and the most conservative definition identified a prevalence among this UK population-based cohort of older women of 11.6%. This differed from the previous work in other studies, as in these the study population was determined by participants who had foot pain, rather than exploring prevalence within a general population not defined by the presence or absence of foot pain.

7.6. Future work

7.6.1. Implications for clinical practice

The prevalence established in the UK based population of older women is important. Novel to the research in the field generated for this thesis is the prevalence of radiographic foot osteoarthritis in a UK based population. Despite the work of Roddy et al. (2013) describing osteoarthritis in a UK based population, it is important to consider that this was a symptomatic population. Foot pain has been described at a level of detail which appears not to have been reported for a single research study, with a large number of different pain variables giving an important relative context to each definition. Additionally, disabling foot pain has been identified from its various definitions and from the review of literature this appears to be the first presentation of all the definitions of disabling foot pain within the context of a study population not defined by presence or absence of pain, rather than prevalence within a symptomatic population. Finally, painful foot osteoarthritis among a sample of a UK based general population of women has been presented and importantly shown that participants with an earlier diagnosis of radiographic osteoarthritis went on to demonstrate foot pain in their follow-up appointment seventeen years later.

The prevalence results established in this thesis provide an important contribution to clinical practice through the large quantity of data on a large sample of participants, where data have been generated to a consistently high level of quality. This enables health and medical professionals to gain an understanding of prevalence and apply this knowledge to be able to estimate the number of pathologically affected patients in the general population. Cultural differences have also been identified through data generated. These appear to exist on a local level with regards to foot pain and should be an important consideration for health and medical professionals when treating patients holistically.

Clinician diagnosed foot pain was surprisingly low and provides an important discovery that the passive joint motions used typically in clinical practice are not adequately capturing foot pain according to the self-reporting by participants. This is not to disqualify this assessment as relevant,

but rather to highlight that clinicians should not rely on this single measure in the diagnosis of foot pain.

Challenges were presented, and although these were identified and solved prior to the evaluation of the x-rays included in this thesis, techniques and skills of radiographic evaluation with the atlas were acquired through consensus or discussion work with no less than two rheumatologists, four radiographers, three podiatrists and a physiotherapist. It would be fair to say that this is not practical for a clinical podiatrist, but was a requirement to ensure the standard of evaluations were high. Despite these challenges, it is important to note that a good level of reliability was demonstrated by a podiatrist in the early stages of the MPhil project (prior to the majority of the consensus and collaborative work) whilst using the LFA.

In order to improve and develop the translation of the atlas from a research derived document to a clinically viable diagnostic tool with widespread uptake among professionals, a guide to the atlas is likely to be the difference between clinical professionals using the atlas and not using the atlas. A guide should provide detail on decision-making only when there is absolute certainty and not by extrapolating visual information from either the atlas or the patient radiographic image being evaluated. Dialogue on the anatomical appearance of a joint should be included which would benefit from the input of an osteology expert. Importantly, regarding the differences between analogue (plain film) and digital (computer software) radiographic images, the advance and incorporation of digital radiography would suggest that a digital version of the atlas would be the most forward-thinking approach. Given these conclusions, the best means of presenting the atlas would be through the development of a mobile software application (ie a mobile app) with a scoring guide for each joint with the ability to input scores for each joint in each projection and a system of flagging each time a joint is considered to be ‘ungradable’ to assist with the interpretation. Development of the atlas with careful use of language and the development of guidelines could be an important research and clinical diagnostic tool, and could revolutionise the way in which osteoarthritis is evaluated.

7.6.2. Implications for future research

It would be a valuable contribution to the field of foot osteoarthritis to further develop research on the basis of the work carried out for this thesis specific to the co-existence of radiographic foot osteoarthritis and foot pain. The co-existence among individual joints where foot pain is the outcome requires development as the baseline data were limited to overall foot pain as described by participants rather than involving a specific reference to joints. Further to this, work should be

carried out to consider the development of a validated template more befitting to the MFPDI foot manikin diagrams when categorising pain more appropriately in relation to joint sites.

This thesis was developed using a well-established cohort of women recruited with no known pathologies between the ages of 69 and 93. The most obvious next stage to follow on from the work in this thesis is to consider men of similar characteristics, and to repeat the same methods of assessment, evaluation and analysis to understand gender differences that may exist. This is an important consideration as it is well known that osteoarthritis, in general, presents as more prevalent among female populations, and this is no different in painful foot osteoarthritis (Roddy et al. 2015).

The Chingford 1000 Women study represents an interesting challenge with demographic characteristics and study design. Although little can be done in terms of changing demography from political, geographical and socio-economic effects, as was the case for the Chingford study, standardised approaches whilst investigating foot osteoarthritis are likely to benefit future longitudinal data in prospective studies and to improve on the heterogeneity existing as a lack of consensus on definitions. Where prospective studies are being set-up with an interest in or focus on the foot and specifically, with the view to incorporate radiographic diagnoses in the design, the field of research could benefit from longitudinal data using digital radiographic equipment recorded using computer software.

The presentation of radiographic foot osteoarthritis has been defined, and so future work should consider disease presence patterns of osteoarthritis in greater detail. The consideration of additional joints will allow the order of prevalence to be determined and provide better scope of foundational epidemiological work in the foot. It is evident that research in foot osteoarthritis is less developed than knee, hip or hand osteoarthritis. More work should focus on developing the body of research using longitudinal data where participant recruitment inclusion criteria are more specific to target groups, to improve sample sizes and therefore statistical power.

Research in foot osteoarthritis should also be proactive in not relying upon semi-quantitative measures. For instance, quantitative measures using joint space width are worth considering, particularly given the lack of benefit or meaning observed through the work of the thesis in considering foot osteoarthritis collectively with polyarticular evaluated radiographic osteoarthritis. The move to quantitative measures will undoubtedly improve subjectivity, particularly considering

the previous discussion (section 7.5.2.) that the 'best-fit' approach of an atlas like the LFA can result in investigators evaluating overall appearance rather than the radiographic features. Of note also, are the recent developments whereby structural osteoarthritis can be considered in the earlier stages due to the availability of evaluating soft tissue changes, which is more encompassing of joint structures in novel terms where the joint is considered an organ. Although in its infancy within structural osteoarthritis with studies using small sample sizes, this would likely provide detailed understanding of the changes in structural foot osteoarthritis and bring the foot into line with the more detailed understanding of the hip and knee.

7.7. Conclusions

The research presented in this thesis has met a need within the current body of research and has advanced knowledge and understanding of radiographic osteoarthritis and foot pain, which was determined through detailed review of the literature. The need to consider the co-existence of radiographic foot osteoarthritis and foot pain within a population was not determined through previous characteristics of pain but by using a general population irrespective of presence or absence of foot pain. The prevalence of radiographic foot osteoarthritis and of foot pain was found to be consistent with preceding research, and provided validation for subsequent work on co-existence and incidence among UK women.

Key to this thesis has been the discovery that the definitions used in research on foot osteoarthritis and foot pain are of critical importance. The heterogeneity that exists, particularly within foot pain, makes an already difficult study variable more difficult to interpret in the context of other research results. Foot osteoarthritis is no different in requiring a standardised definition, however, it is evident through methods of previous research studies that radiographic features are one element of standardisation that are generally accepted when using radiographic imaging. This thesis has been carried out in order to explore definitions and provide a research based approach to establish best methods for presenting epidemiological research in radiographic foot osteoarthritis and foot pain whilst considering co-existence using cross-sectional and longitudinal methods to determine prevalence and incidence.

In summary, the variable selected to identify current foot pain demonstrated foot pain among one in five women. Radiographic foot osteoarthritis was demonstrated to exist in one in ten women for polyarticular evaluated foot osteoarthritis. Co-existing radiographic foot osteoarthritis and foot pain was found to exist in one in five women with one in ten women having co-existing radiographic foot osteoarthritis and disabling foot pain. Incidence of radiographic osteoarthritis over a seventeen year

period was found to be low, but was higher in the right foot and a low number of participants went on to develop foot pain when they had presence of radiographic foot osteoarthritis at baseline.

The data provide clinicians with a good basis for understanding the prevalence and incidence of radiographic foot osteoarthritis and foot pain (and middle-aged prevalence) among older British women. Further to this, knowing the distribution and presentation of radiographic osteoarthritis with pain symptoms will enable better targeted treatment strategies for clinicians. Appropriate measures of radiographic foot osteoarthritis and foot pain have been identified and good reliability of a podiatrist using the LFA have been established. The exploration of foot osteoarthritis with the foot pain characteristic is a complex one, and represents future challenges in research. However, the emergence of good foundational epidemiological work in this area will help to expand the breadth of knowledge regarding the disease and its symptoms within the foot.

Finally, recommendations have been provided for the development of the understanding and knowledge of epidemiology of radiographic foot osteoarthritis and foot pain. Recommendations have also been made for the development of the LFA to improve the evaluation techniques. This could facilitate greater uptake of the atlas by clinicians and improve the standardisation of the atlas, which would likely improve user reliability in both research and clinical contexts.

Appendix 1 LFA

Radiographic classification of osteoarthritis in commonly affected joints of the foot

Supplementary data: atlas of radiographic images

S1. Scoring system
S2. First metatarso-phalangeal joint (dorsal): osteophytes
S3. First metatarso-phalangeal joint (lateral): osteophytes
S4. First metatarso-phalangeal joint (dorsal): joint space narrowing
S5. First metatarso-phalangeal joint (lateral): joint space narrowing
S6. First cuneo-metatarsal joint (dorsal): osteophytes
S7. First cuneo-metatarsal joint (lateral): osteophytes
S8. First cuneo-metatarsal joint (dorsal): joint space narrowing
S9. First cuneo-metatarsal joint (lateral): joint space narrowing
S10. Second cuneo-metatarsal joint (dorsal): osteophytes
S11. Second cuneo-metatarsal joint (lateral): osteophytes
S12. Second cuneo-metatarsal joint (dorsal): joint space narrowing
S13. Second cuneo-metatarsal joint (lateral): joint space narrowing
S14. Navicular-first cuneiform joint (dorsal): osteophytes
S15. Navicular-first cuneiform joint (lateral): osteophytes
S14. Navicular-first cuneiform joint (dorsal): joint space narrowing
S15. Navicular-first cuneiform joint (lateral): joint space narrowing
S16. Talo-navicular joint (lateral): osteophytes
S17. Talo-navicular joint (dorsal): joint space narrowing
S18. Talo-navicular joint (lateral): joint space narrowing

Scoring system

Osteophytes

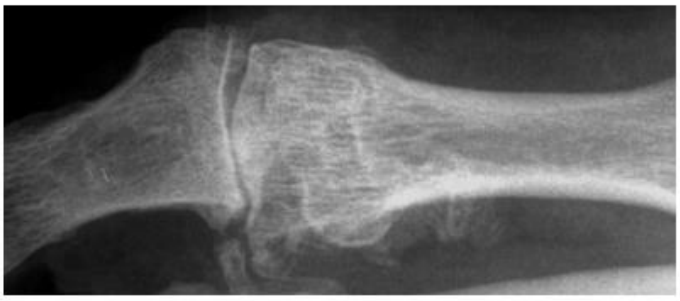
0	absent
1	small
2	moderate
3	severe

Joint space narrowing

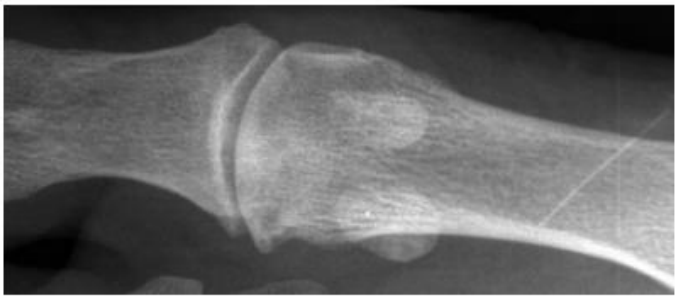
0	none
1	definite
2	severe
3	joint fusion at at least one point

Case definition of foot osteoarthritis in individual joints

Radiographic OA can be considered to be present if a score of 2 or above is documented for *either* osteophytes or joint space narrowing, from *either* the dorso-plantar or lateral view



3



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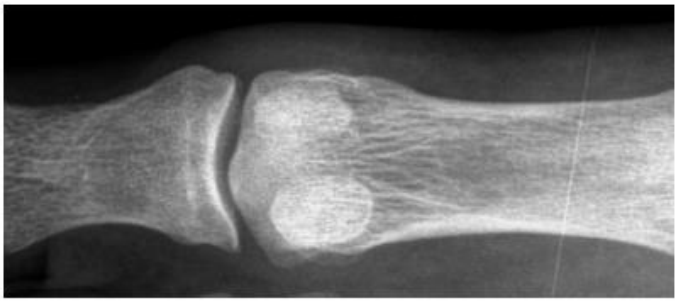

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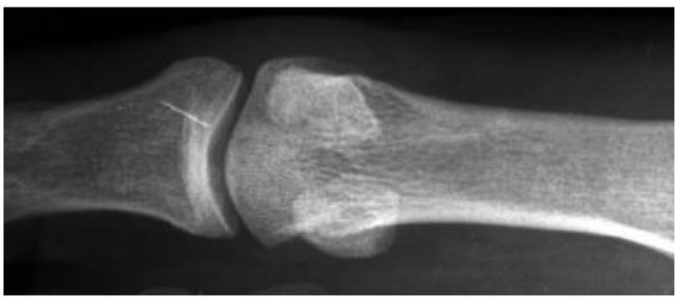
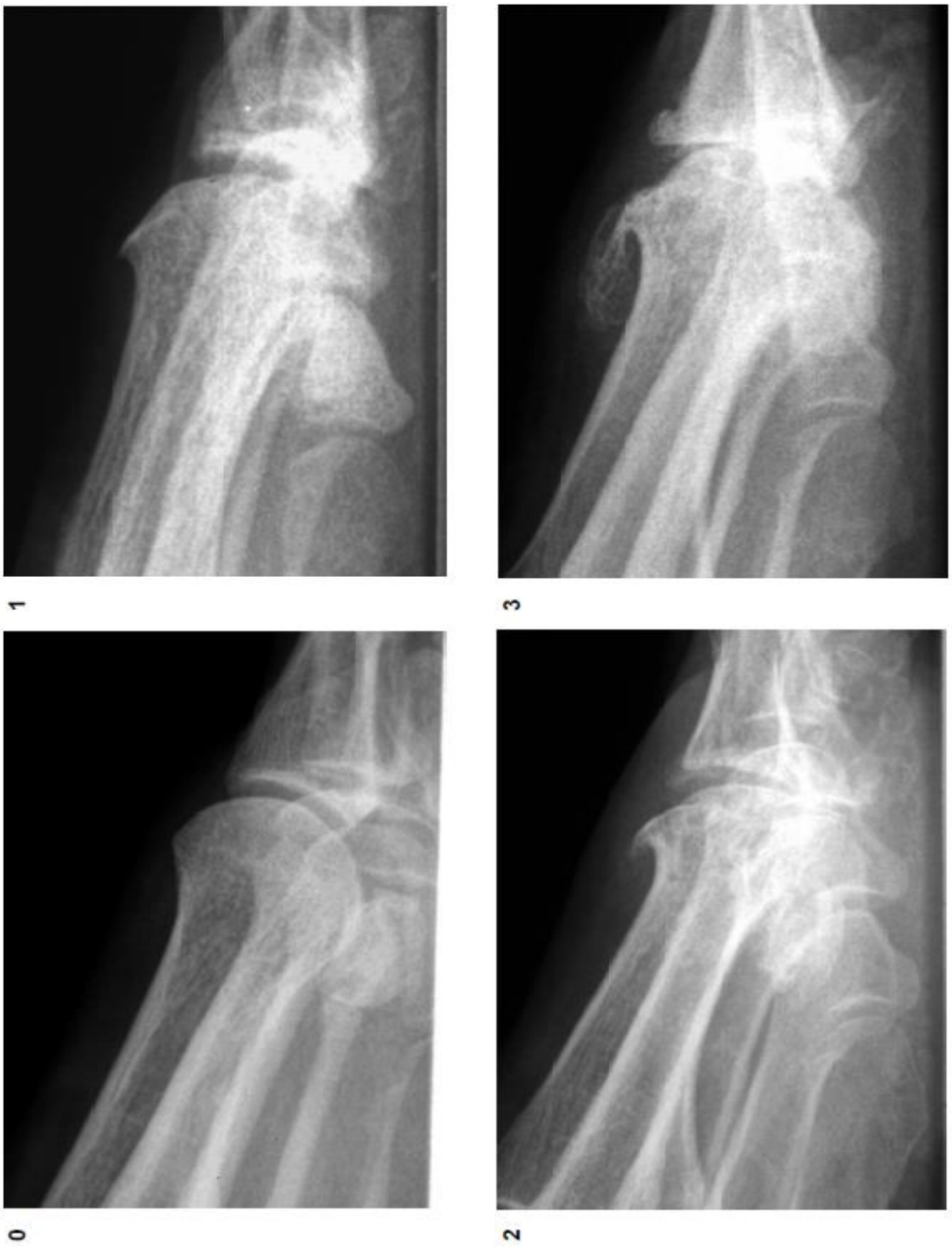
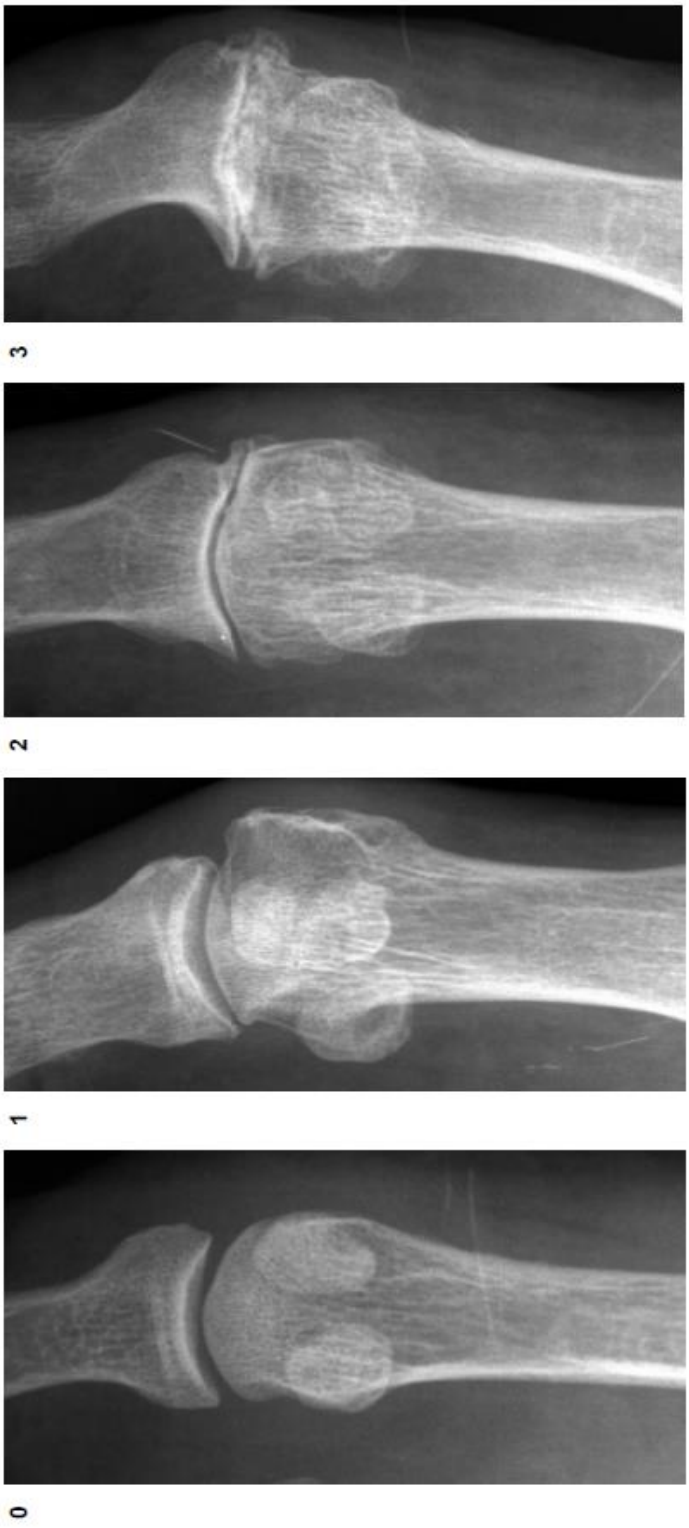


0

First metatarso-phalangeal joint (dorsal): osteophytes

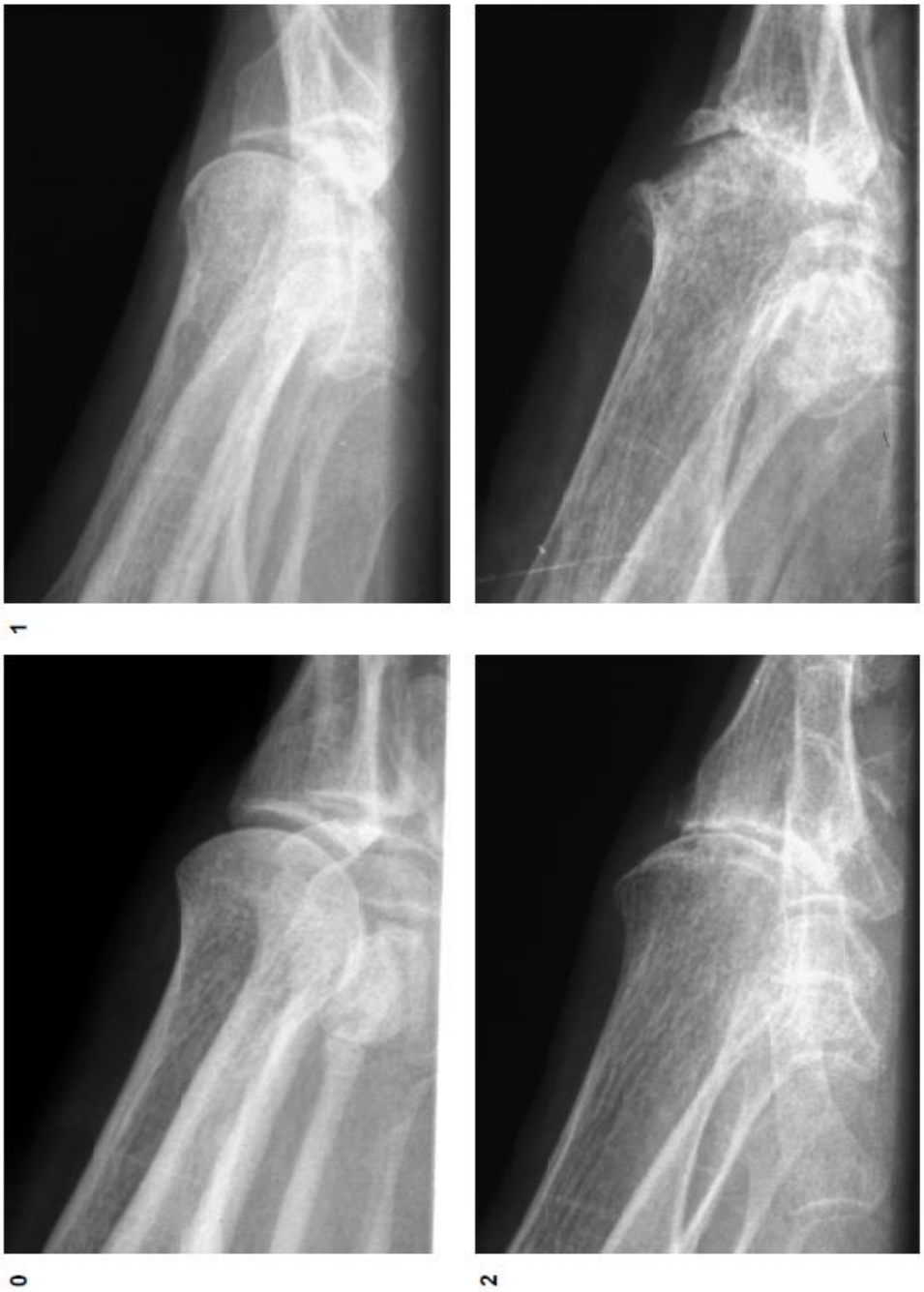
2


1
3
0
2
First metatarso-phalangeal joint (lateral): osteophytes
3

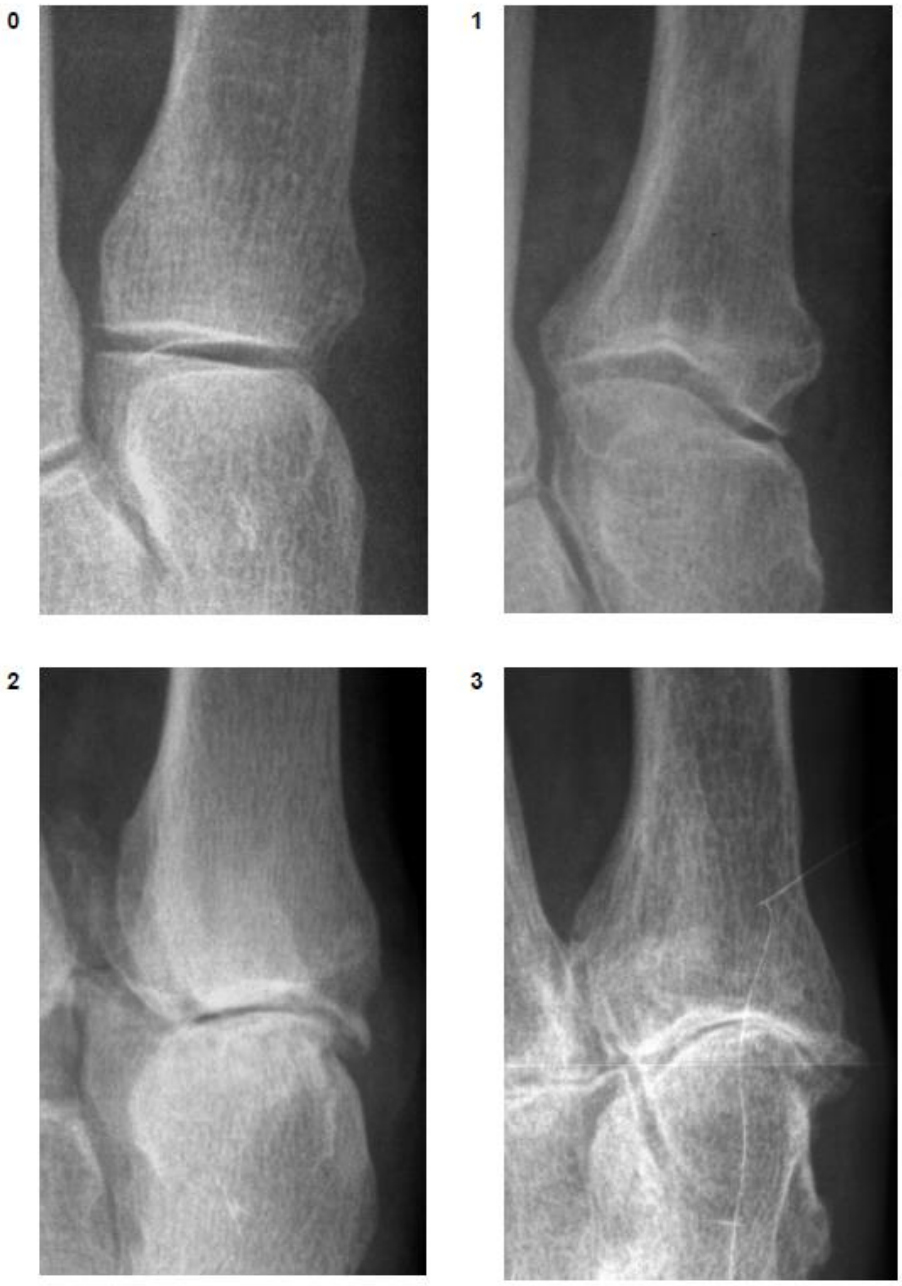


First metatarso-phalangeal joint (dorsal): joint space narrowing

4

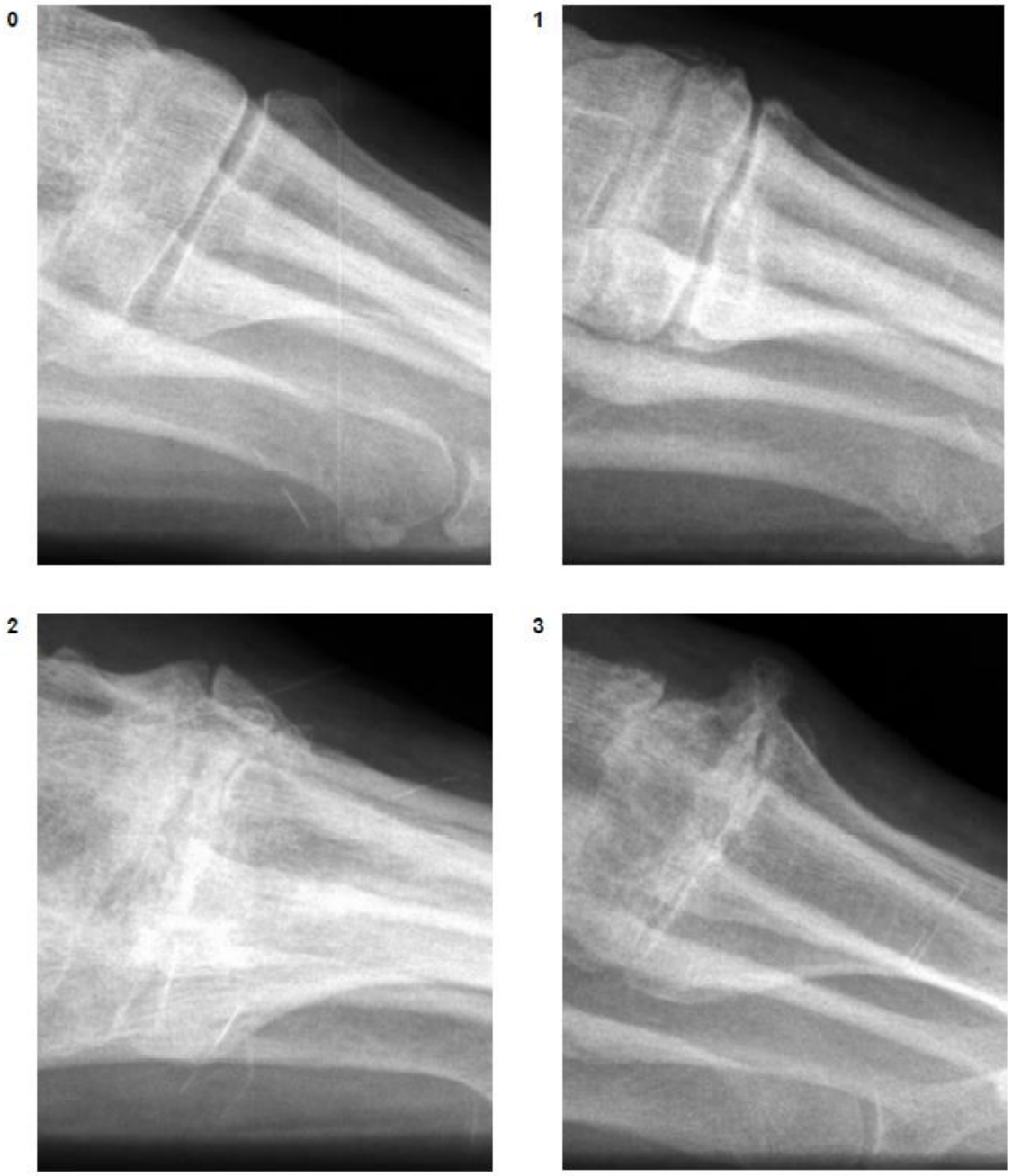

0
1
2
First metatarso-phalangeal joint (lateral): joint space narrowing

5



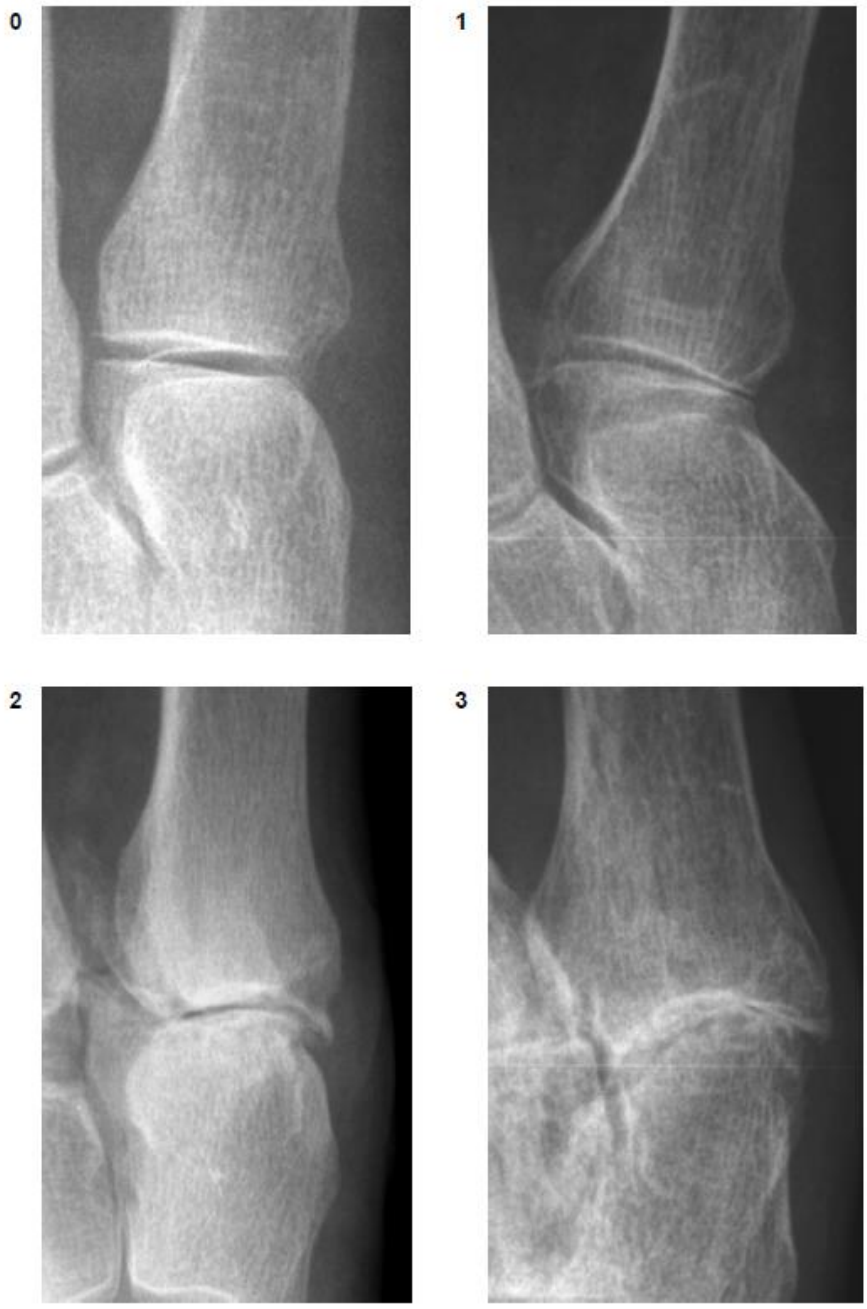
First cuneo-metatarsal joint (dorsal): osteophytes

6



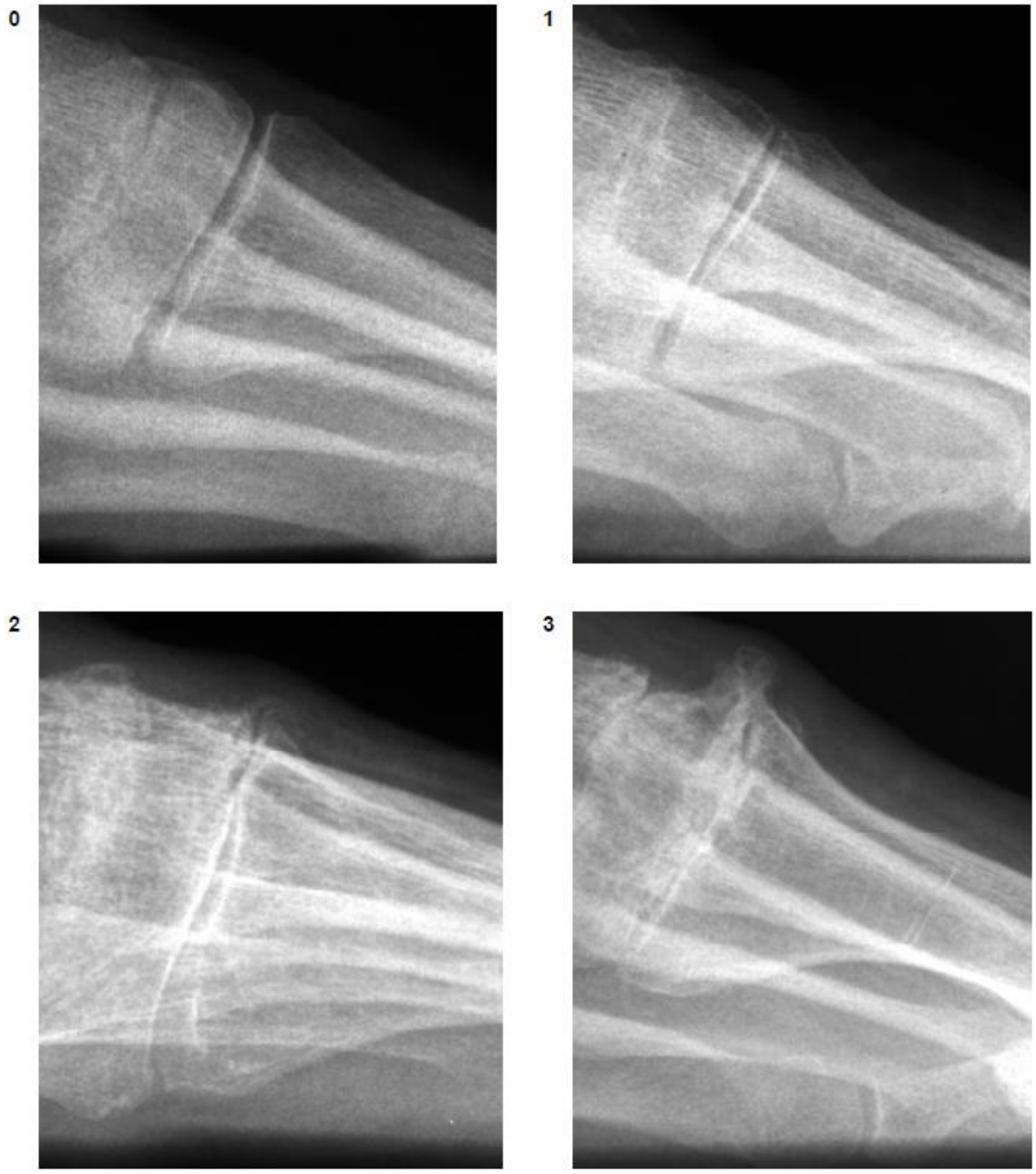
First cuneo-metatarsal joint (lateral): osteophytes

7



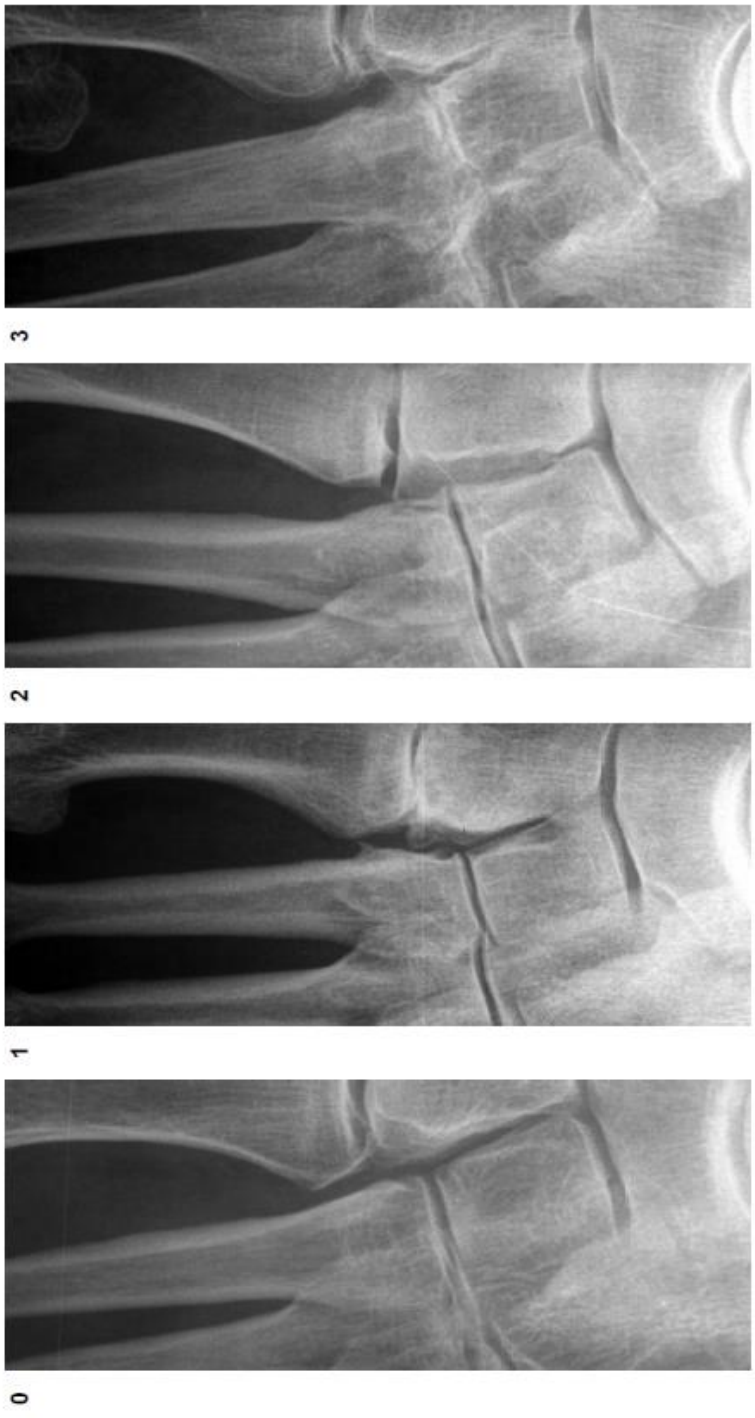
First cuneo-metatarsal joint (dorsal): joint space narrowing

8



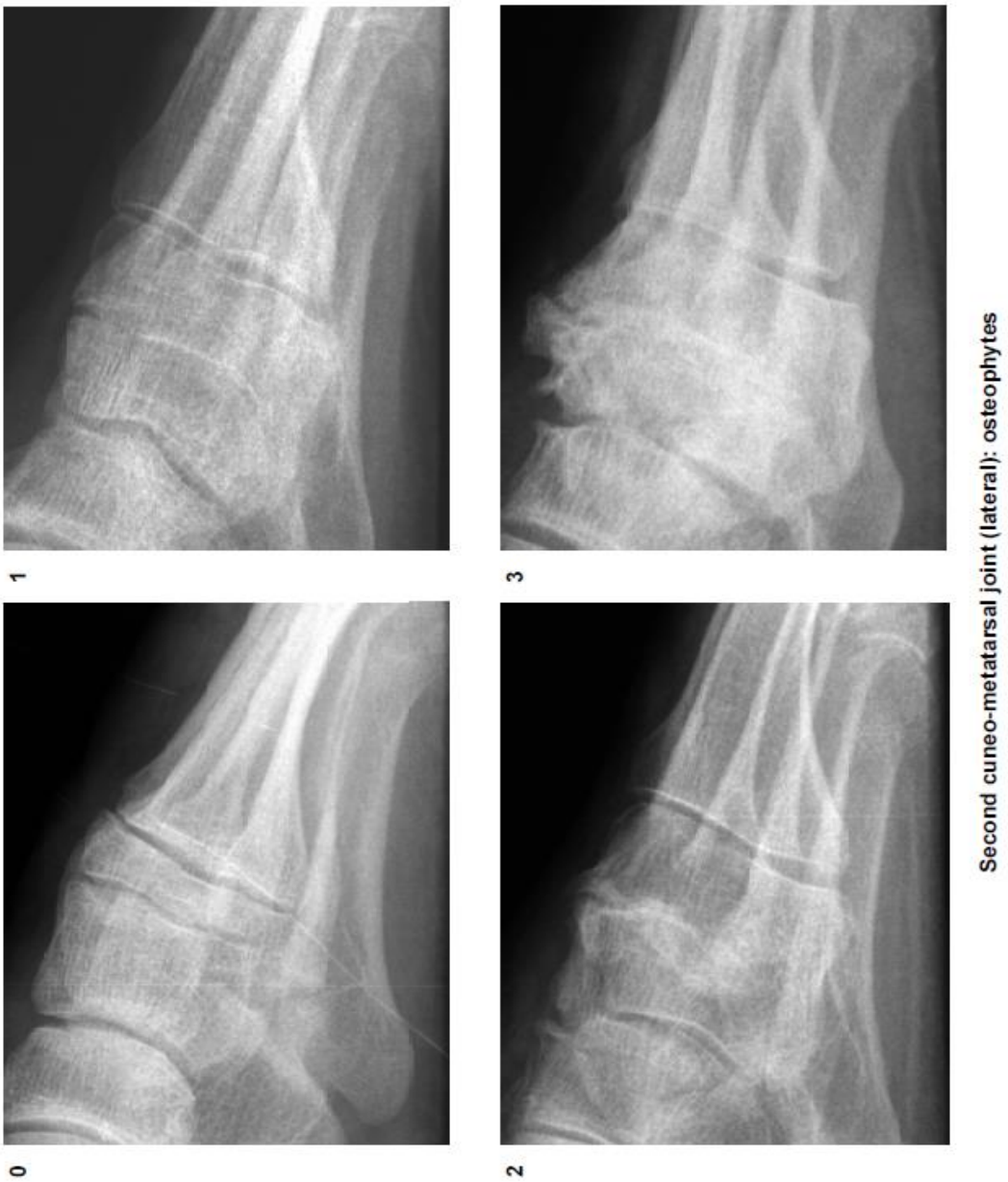
First cuneo-metatarsal joint (lateral): joint space narrowing

9



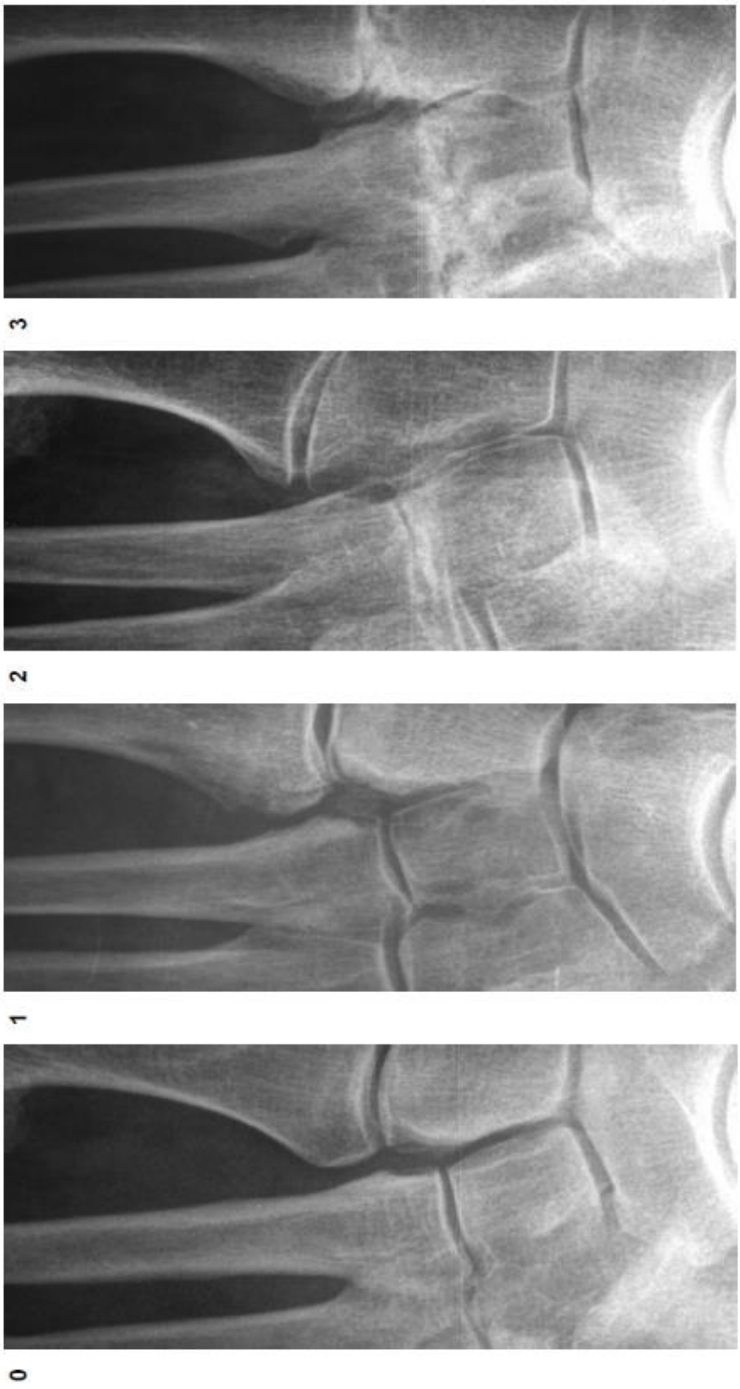
Second cuneo-metatarsal joint (dorsal): osteophytes

10



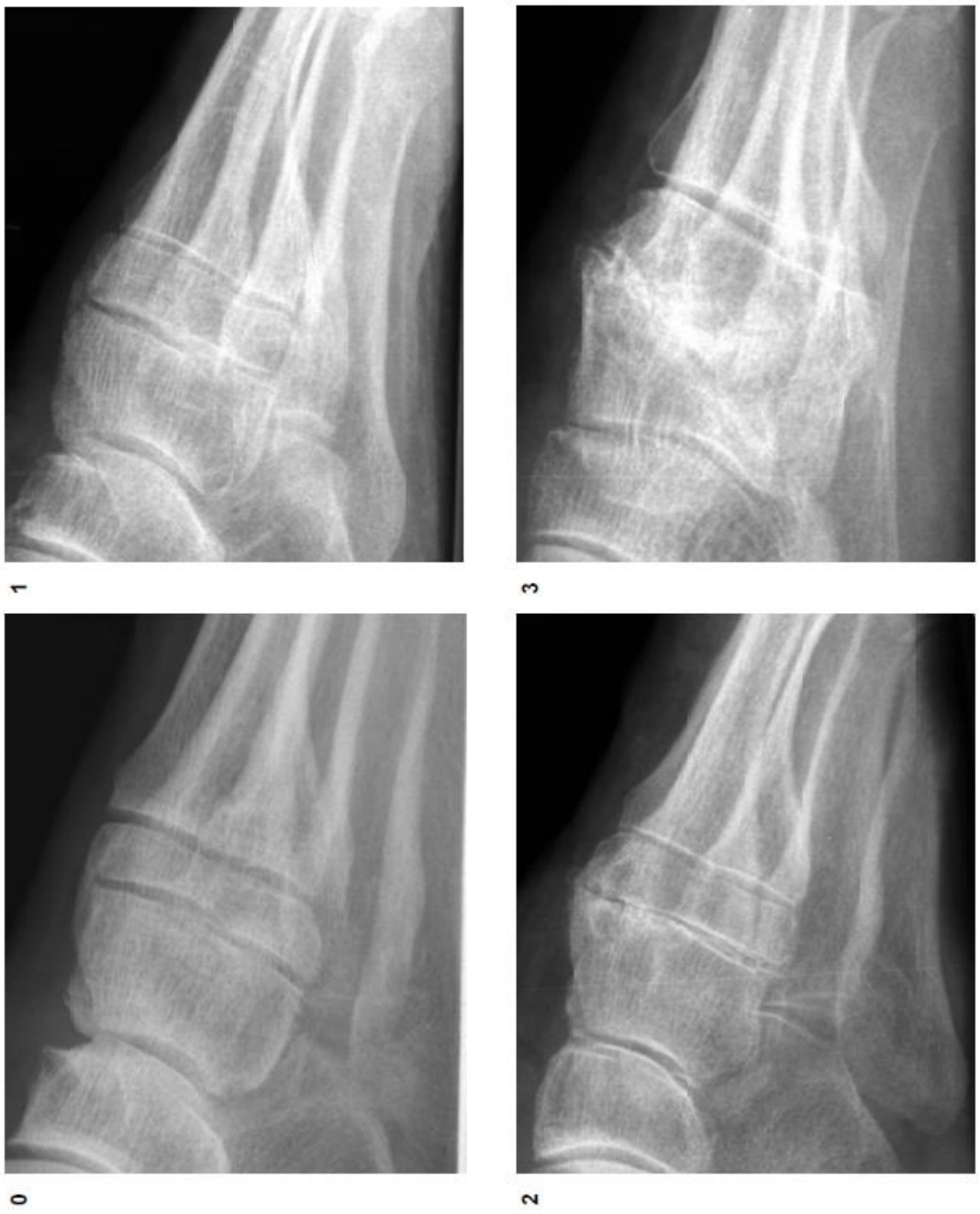
Second cuneo-metatarsal joint (lateral): osteophytes

11



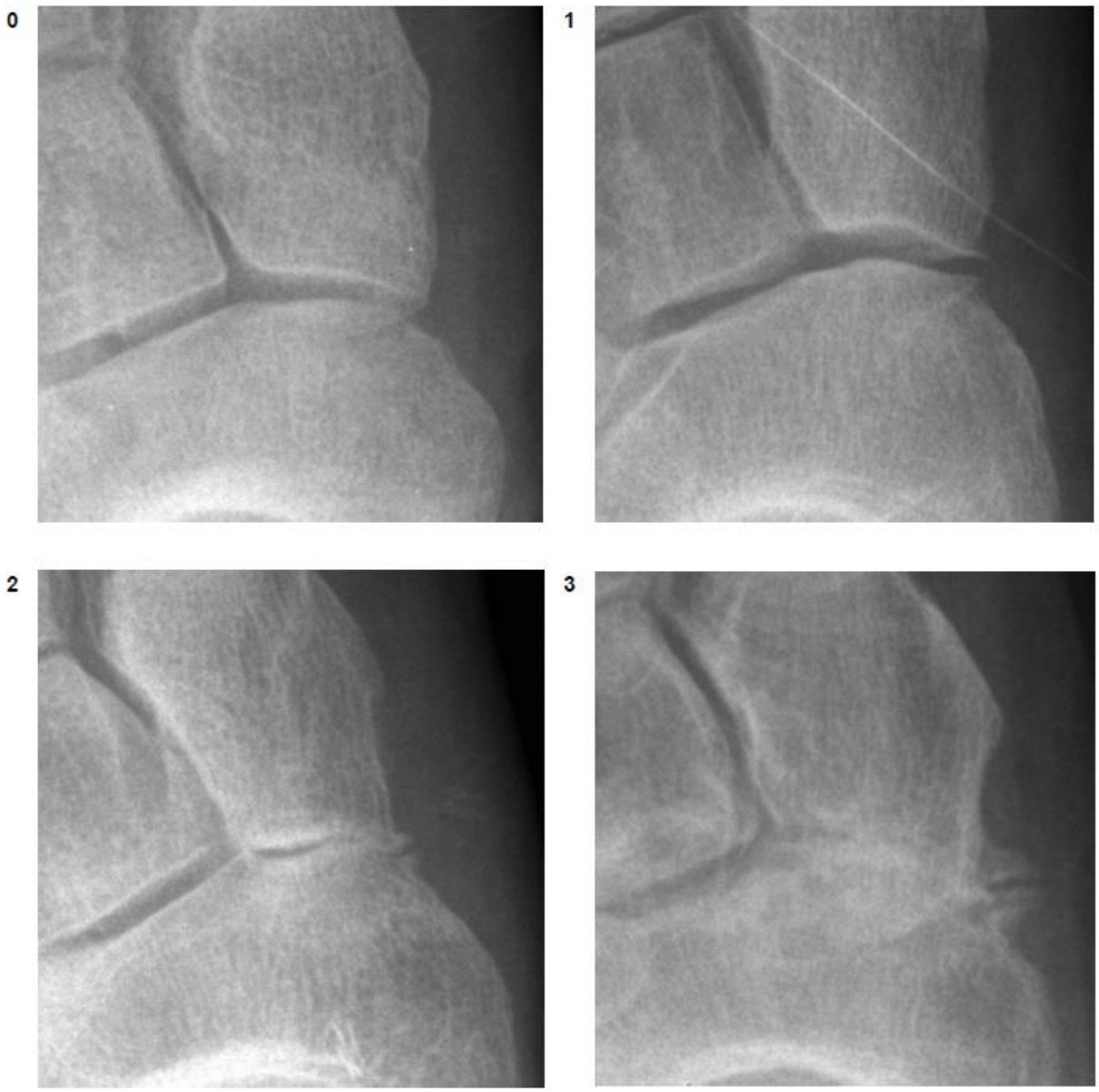
Second cuneo-metatarsal joint (dorsal): joint space narrowing

12



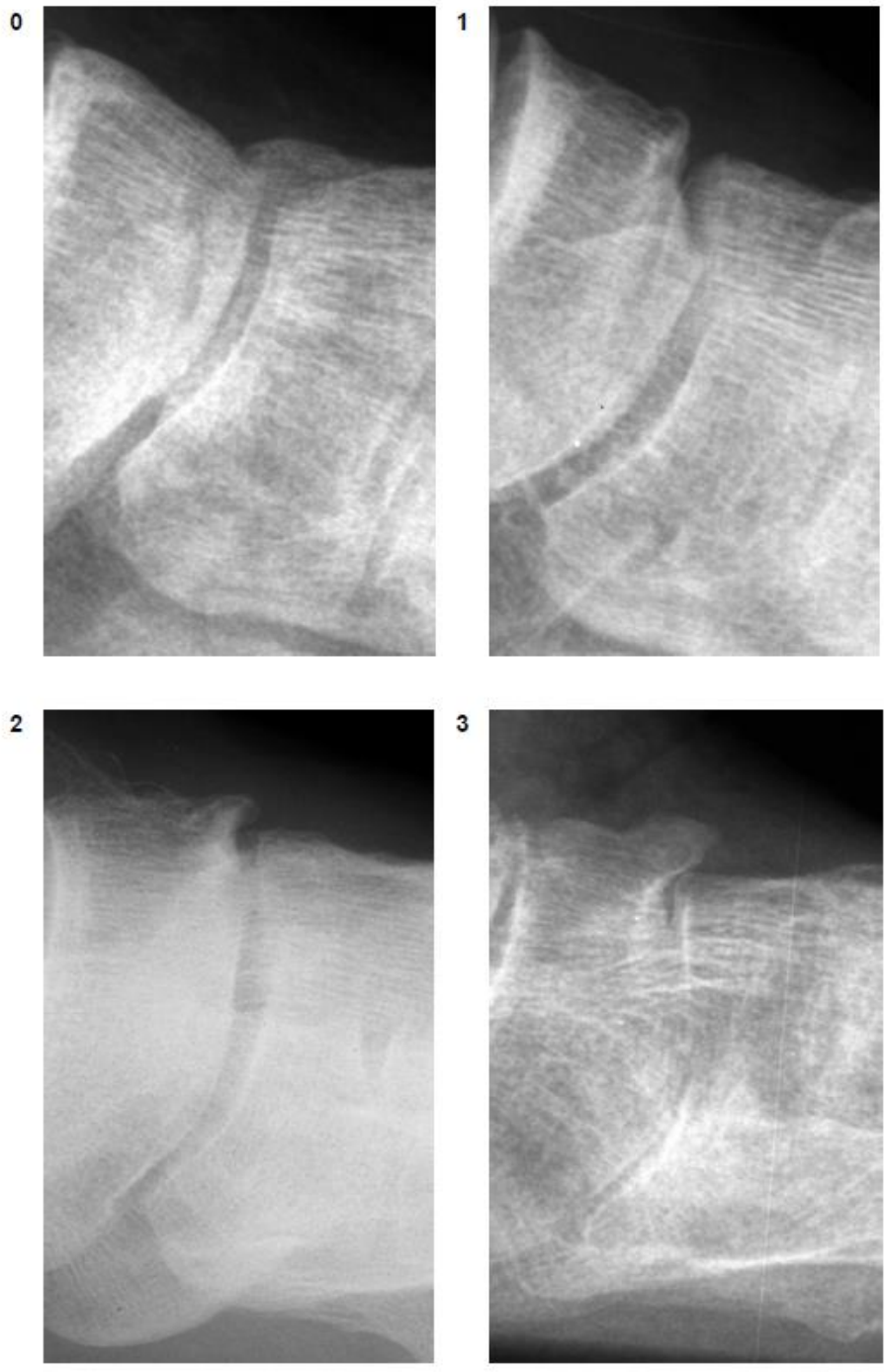
Second cuneo-metatarsal joint (lateral): joint space narrowing

13



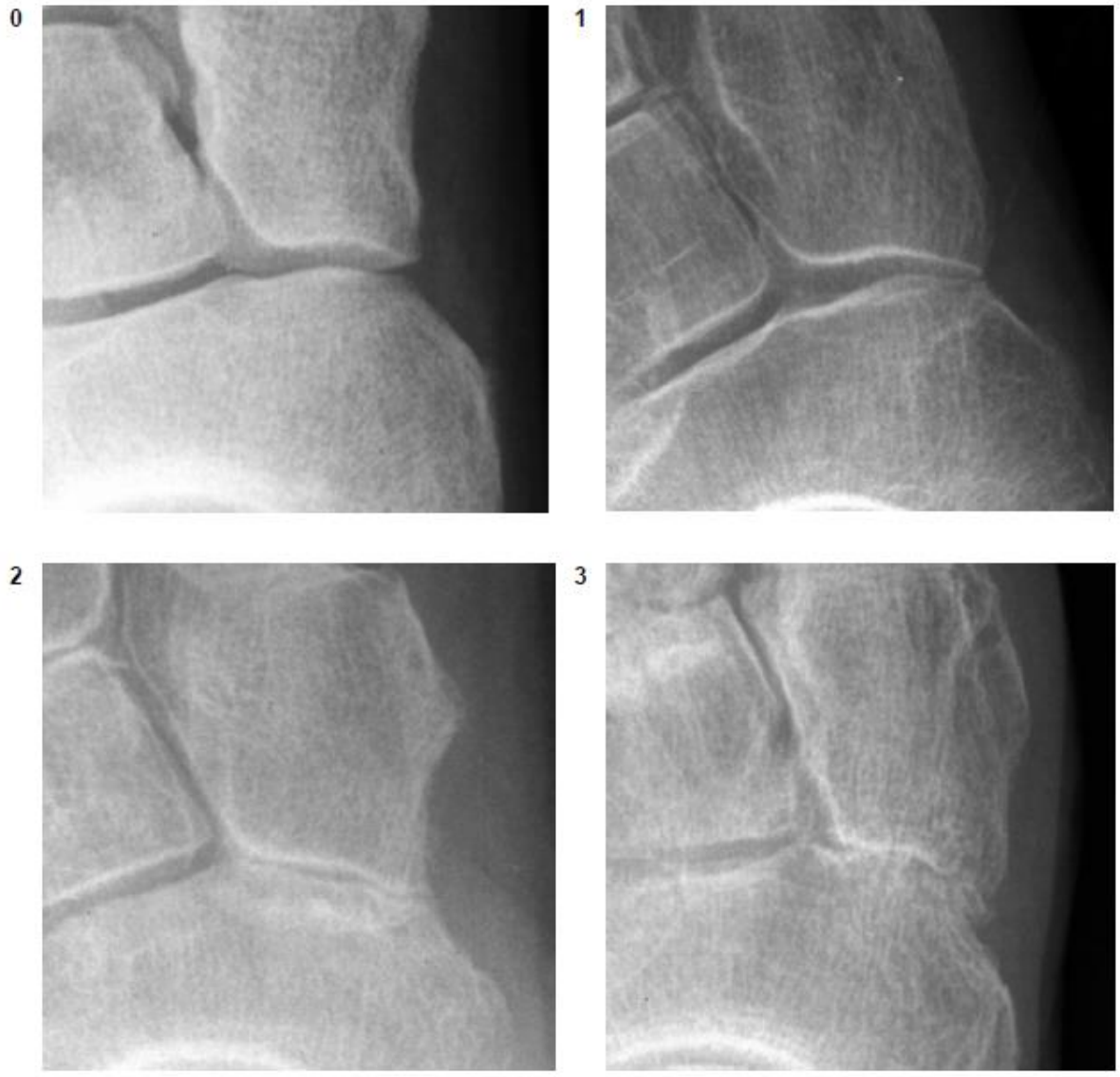
Navicular-first cuneiform joint (dorsal): osteophytes

14



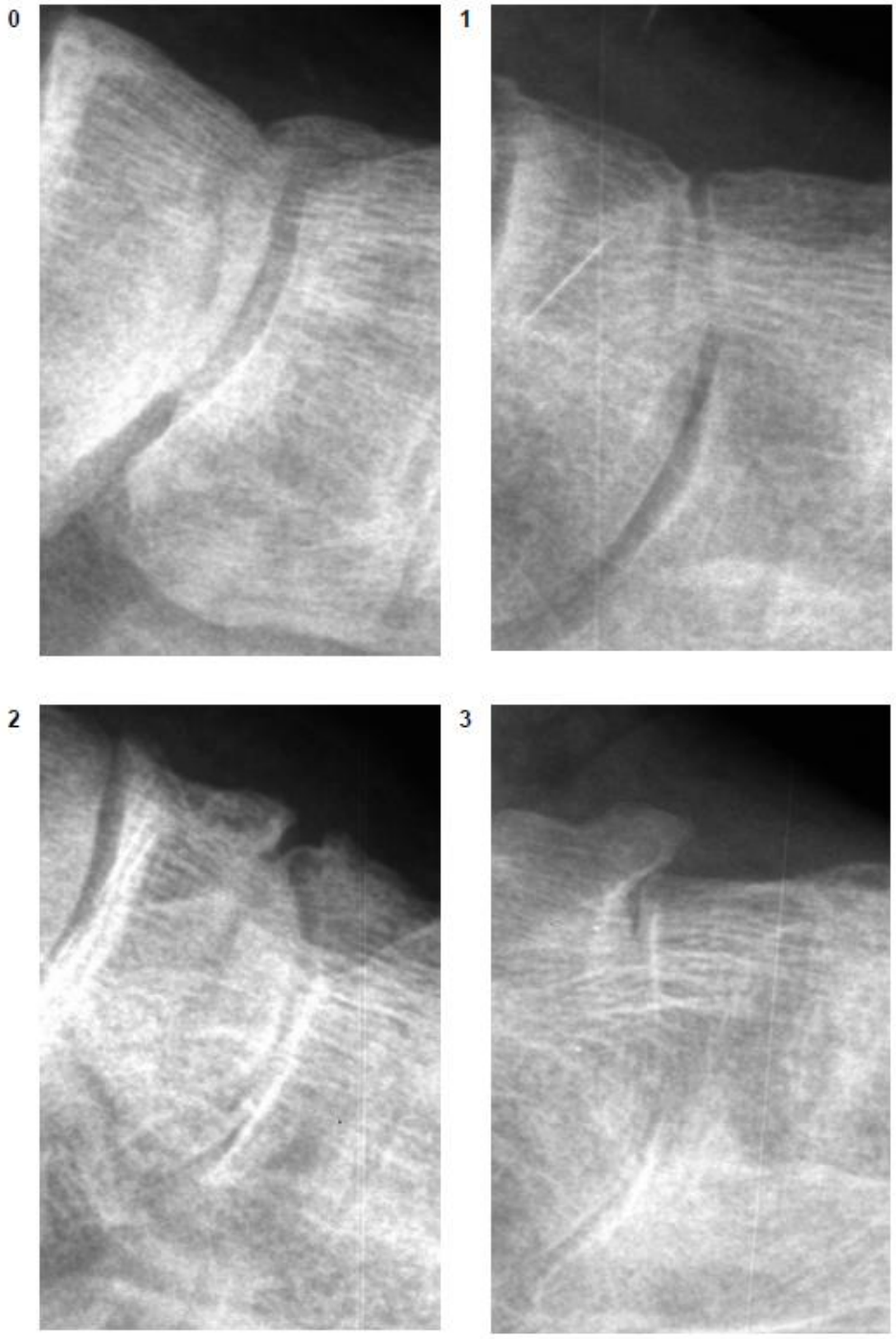
Navicular-first cuneiform joint (lateral): osteophytes

15

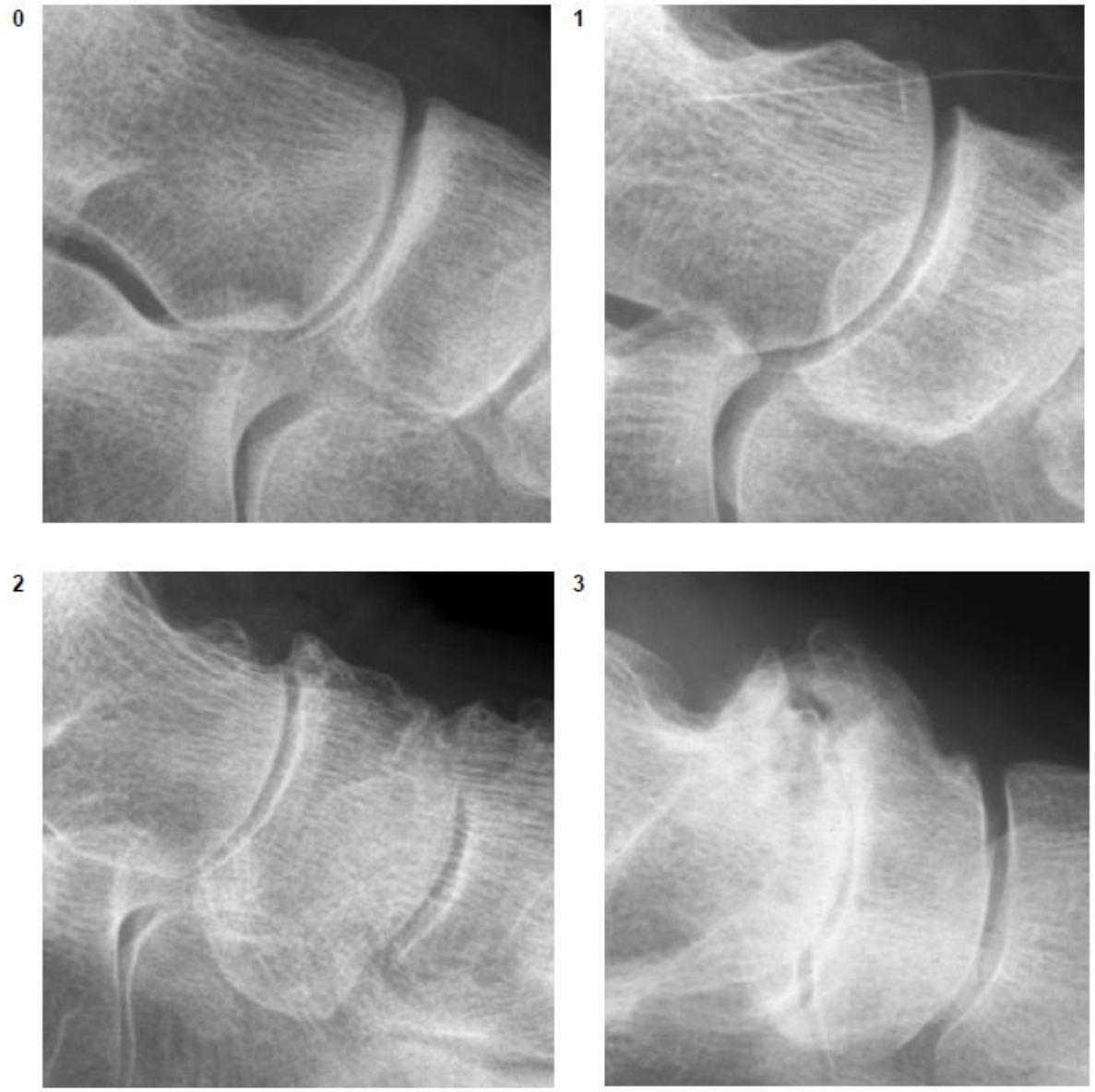


Navicular-first cuneiform joint (dorsal): joint space narrowing

16

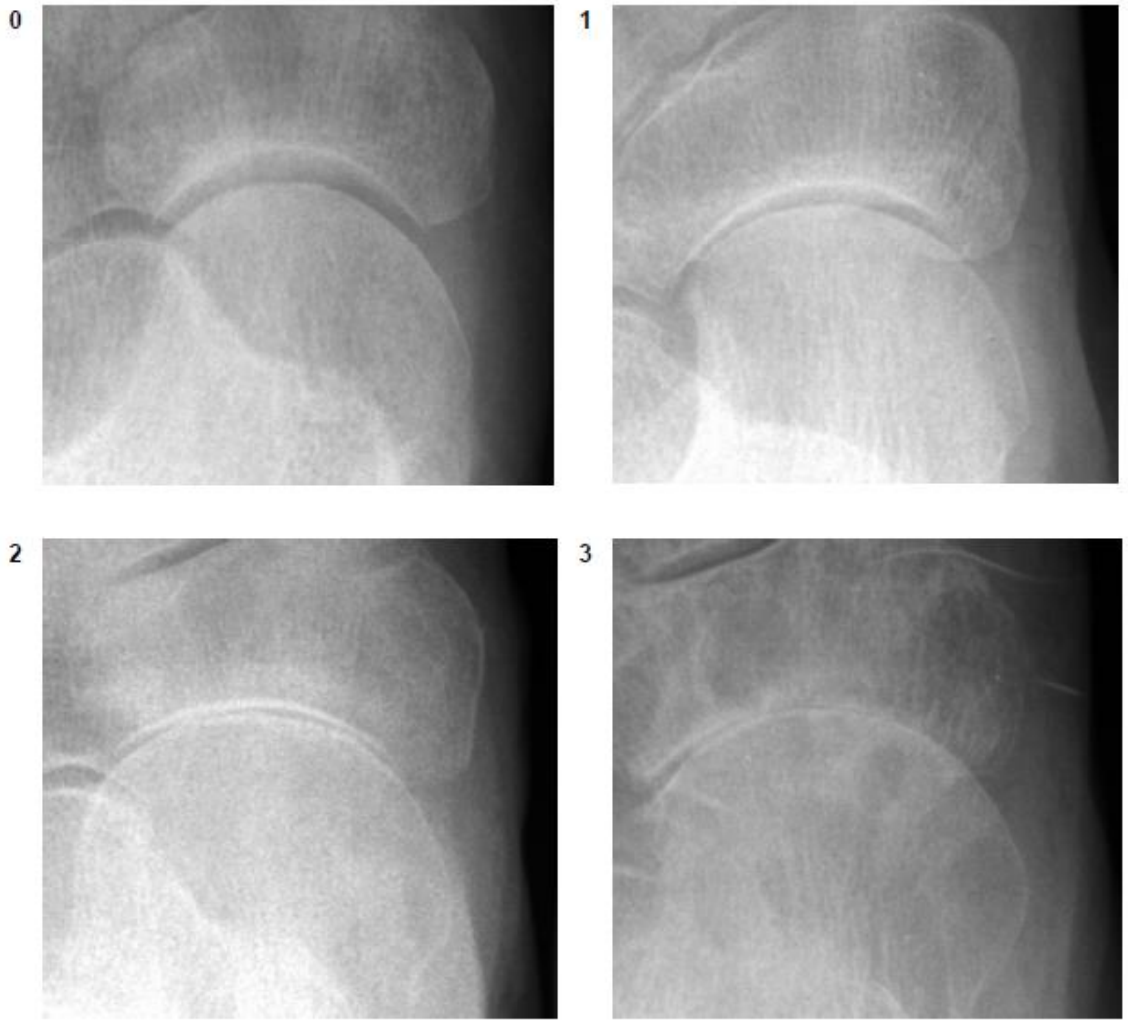


Navicular-first cuneiform joint (lateral): joint space narrowing 17



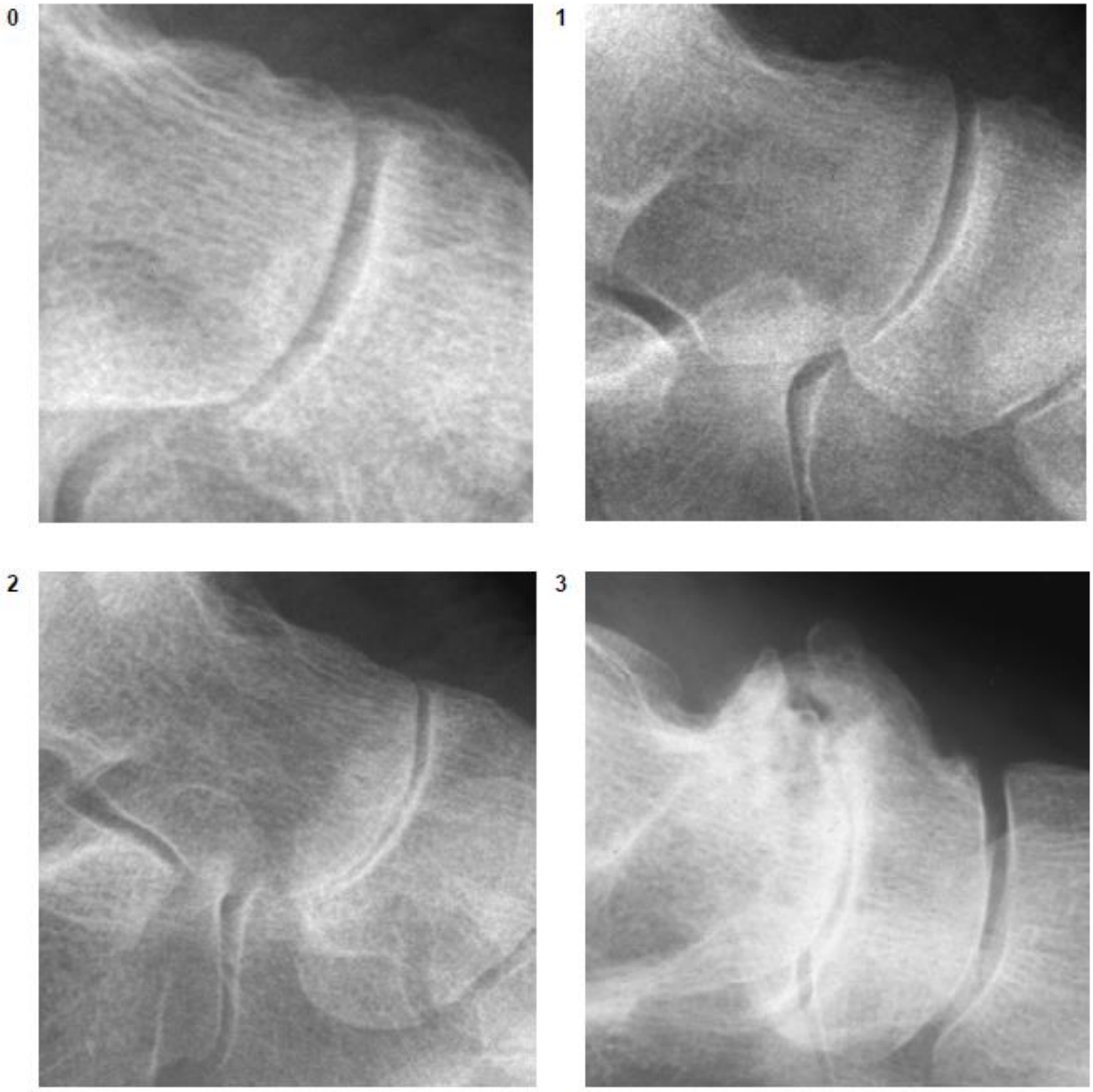
Talo-navicular joint (lateral): osteophytes

18



Talo-navicular joint (dorsal): joint space narrowing

19



Talo-navicular joint (lateral): joint space narrowing

20

Appendix 2 Example search strategy using PICO chart for literature review (Cluett 2005)

Research

Developing clinically focused questions for quantitative research

Initial idea: *'what is the prevalence of osteoarthritis with co-existing foot pain in the general population?'*

P **Population/patient**	General population (all ages in adulthood)
I **Intervention /focus of questions**	Radiographic, ultrasound, Magnetic resonance imaging
C **Comparison or baseline status**	Foot osteoarthritis and no foot osteoarthritis (Pathological and non-pathological populations)
O **Outcome – end point interested in**	Pain Reliability of radiographic scoring.

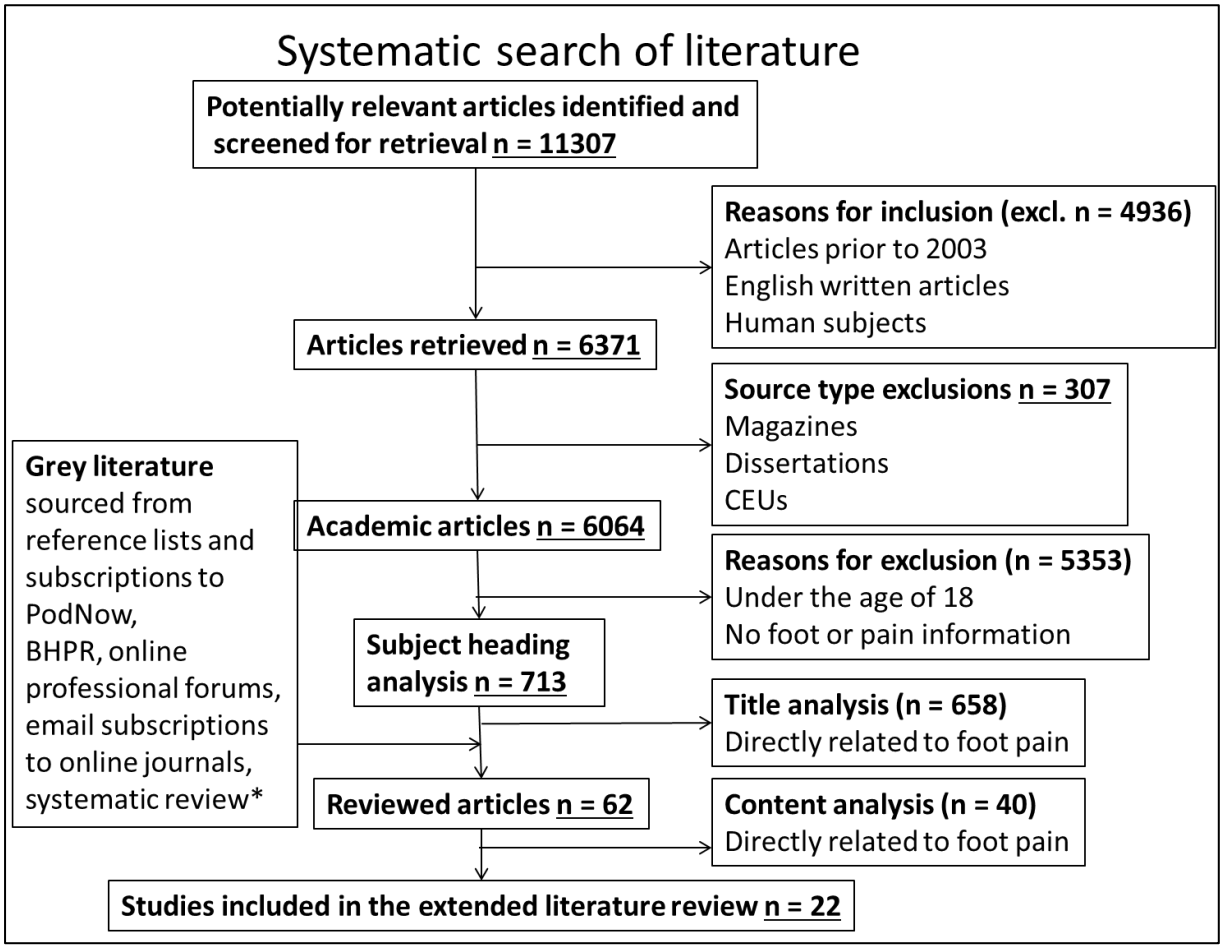
Appendix 2 continued….

Clinical question: 'Are radiographically evaluated structural manifestations of osteoarthritis in the foot of the general population associated with symptomatic OA?'

KEY words	Alternative words
Foot	Feet, toes, digits, ankle, midfoot, forefoot, rearfoot, hindfoot, ray, MTPJ, metatarsophalangeal, interphalangeal joint, cuneo-metatarsal, metatarsocuneiform, cuneonavicular, navicular cuneiform, navicular first cuneiform joint, talonavicular, cubometatarsal, cuneocuboid, cubocuneiform, calcanealcuboid, calcaneocuboid, talocalcaneal, talocalcaneonavicular, cubonavicular, naviculartcuboid, talotibial, subtalar, talocrural, midtarsal, IPJ, MTPJ, CMJ, 2nd CMJ, CNJ, N1stCJ, TNJ, CM, TC, TCN, CN, NC, TT, ST, metatarsal, phalanx, phalanges, cuboid, cuneiform, navicular, talus, calcaneus, tibia, fibula. Additional peer review terms: Pedal
Radiography	Radiographical, radiographic, radiographically, radiological, radiologic, radiologically, radiology, roentgenology, roentgenological, roentgenologically, nuclear, x-ray, imaging, image, grading, graded, plain film, magnetic resonance, MRI, MR, ultrasound, ultrasonography, ultrasonograph, ultrasonographic.
Symptomatic	Painful, pain, swollen, swelling, aching, ache, stiffness, stiff, gelling, gel, arthralgia, erythema, heat Additional peer review terms: Symptom
Osteoarthritis ***OR***	OA, osteoarthritic, Osteoarthrosis, Arthropathy, osteoarthropathy, arthritis, degenerative joint, Hallux Limitus, Hallux Rigidus, Hallux Valgus, regenerative, joint failure.
Structure change in osteoarthritis	Disease, morphology, morphological, morphologically, cellular, degradation, degenerative, degeneration, regenerative, regeneration, subchondral cyst, joint space narrowing, joint space width, osteophyte, osteophytes, osteophytic, syovium, synovial, cartilage, hyaline cartilage, articular cartilage, osteochondrophyte, bone marrow, bone marrow lesions, bone marrow oedema Additional peer review terms: Pathological, pathology, pathologically, clinical, clinically, manifestation, marker, markers, features
General population	People, humans, human, subjects, subject, adults, adult, persons, person, participants, participant, cohort, citizens, citizen, public, residents, residential, inhabitant, inhabitants, community, village (retirement), elderly, geriatric, pensioners, pensioner, young, adolescence, adolescents, teenagers, middle aged, middle-aged, retired, retiree

Appendix 3 Example Flow chart of results of literature review presented

Appendix 1 and 2 supplied the main search strategy from which separate searches were carried out on foot pain and foot osteoarthritis as the combined foot osteoarthritis and foot pain demonstrated a very small body of research. Databases that were used included CINAHL, MedLine, Embase and Amed of which the latter produced no results in combined osteoarthritis and pain in the foot searchs. Below are the results and strategy to acquiring the literature.



Appendix 4 Pain definitions

Dunn et al. 2004	**Tool:** N/A **Location:** any of the foot or ankle joints **Time:** Last 4 weeks **Symptoms:** Pain or discomfort **Positive selection criteria:** 'Yes' followed by a question to locate pain by circling area (both unilateral and bilateral pain)
Cho et al. 2009	**Tool:** Korean FSHQ **Location:** Feet **Time:** Last week – never/occasionally/fairly often/very often/always **Symptoms:** Aches or pains **Positive selection criteria:** Fairly often/very often/always
Mickle et al. 2010	**Tool:** MFDPI-17 **Location:** Foot **Time:** Last month **Symptoms:** Pain only **Positive selection criteria:** 1 or more in MFPDI
Thomas et al. 2004	**Tool:** N/A **Location:** Full body **Time:** Past month for one day or longer **Symptoms:** Pain only **Positive selection criteria:** Positive responses were asked to locate pain by shading in a manikin which defined areas by a transparent template with borders.
Mickle et al. 2011	**Tool:** MFPDI-17 **Location:** Foot **Time:** Last month **Symptoms:** Pain only **Positive selection criteria:** 1 or more of some/most/every day. **Disabling foot pain positive selection:** 1 or more of most/every day.
Leveille et al. 2008 MOBILIZE	**Tool:** McGill Pain Map (pain location)/4 item Brief Pain Inventory (BPI) (pain severity)/7 item BPI + additional questions (pain interference/impact) **Location:** Full body **Time:** BPI-4 – current & more than a week or 2/BPI-7 – N/A/McGill – Last week **Symptoms:** Pain only **Positive selection criteria:** Unknown
Hill et al. 2008	**Tool:** N/A (question)/Framingham Study Foot Map **Location:** Foot **Time:** Most days **Symptoms:** Pain, aching or stiffness **Positive selection criteria:** 'Yes' followed by locating pain on a foot map (diagram)
Buchman et al. 2010	**Tool:** N/A **Location:** Back or neck, hands, hips, knees or feet **Time:** Last month for most days

	Symptoms: Pain or aching **Positive selection criteria:** 'Yes' response
Dufour et al. 2009	**Tool:** National Health & Nutrition Examination (NHNE) survey on foot pain/Foot assessment clinical tool (FACT) **Location:** Foot (NHNE) and locations of pain, aching or stiffness were identified by diagram of the plantar & dorsal aspect foot; nails/forefoot/hindfoot/heel/arch/ball (FACT?) **Time:** Most days (NHNE) **Symptoms:** Pain, aching or stiffness (NHNE) **Positive selection criteria:** 'Yes' response (both unilateral & bilateral) (NHNE)
Badlissi et al. 2005	**Tool:** N/A **Location:** Foot **Time:** Last week **Symptoms:** Aches or pains **Positive selection criteria:** Positive response i.e. 'Yes'
Garrow et al. 2004	**Tool:** N/A & MFPDI (disabling foot pain only) **Location:** Foot and pain was located using 3 diagrams of each foot. **Time:** One day in the last month **Symptoms:** Pain only **Positive selection criteria:** Positive response. Disabling foot pain – at least one pain related disability in the foot.
Menz et al. 2005	**Tool:** MFPDI -17 (disabling foot pain only) **Location:** Foot. An interview administered questionnaire for establishing pain location was also used. **Time:** Current foot pain in the last month **Symptoms:** Pain only **Positive selection criteria:** At least one disability item.
Roddy et al. 2011	**Tool:** Health survey questionnaire (HSQ)& region pain survey questionnaire (RPSQ) **Location:** Foot **Time:** Current (as data were recorded at 2 time points) **Symptoms:** Pain (?) **Positive selection criteria:** Positive response to foot pain item in both HSQ & RPSQ
Menz et al. 2011	**Tool:** MFPDI-19 (Disabling foot pain only) **Location:** Foot **Time:** Most/every day(s) of the last month. **Symptoms:** Pain only **Positive selection criteria:** 1/10 or more from the functional items Garrow et al. 2000 (proven to be the best definition for MFPDI).
Abhishek et al. 2010	**Tool:** Roddy et al. 2009 **Location:** Hallux **Time:** Most days of a month for at least 1 month in the previous year **Symptoms:** Pain **Positive selection criteria:** Positive response i.e. 'Yes'

Menz et al. 2005	**Tool:** MFPDI-19 & Garrow et al. 2004 (both disabling foot pain) **Location:** Foot. Specific location was documented. **Time:** Some point in the last month and current pain. Duration was documented **Symptoms:** Pain only **Positive selection criteria:** One MFPDI item & positive response to pain question.
Menz et al. 2011	**Tool:** MFPDI-17 (HRQoL foot specific question documented using MFPDI), Health Survey Questionnaire (HSQ) & full body manikin. (Severity of foot pain). **Location:** Foot and areas of any bodily pain were shaded in. **Time:** Last 12 months. One day or longer in the last month (HSQ) **Symptoms:** Pain only **Positive selection criteria:** Unknown for MFPDI/Positive response for HSQ
Munteanu et al. 2012	**Tool:** Assumed temporal pain question, VAS, clinical examination (Impact/interference). **Location:** 1st Metatarsophalangeal joint **Time:** Pain for at least the last 3 months **Symptoms:** 'Symptoms of pain' **Positive selection criteria:** Positive response to temporal question, 20mm out of 100mm on the visual analogue scale (VAS) or pain upon palpation

Key

Article considers disabling foot pain

Appendix 5 Consent form for C1000W study

Title of Project: Chingford 1000 Women Study **Chief Investigator:** Professor Nigel Arden Professor Tim Spector **NRES Committee South Central – Oxford A:** **REC Ref: 13/SC/0168**	Osteoporosis Unit, The Silverthorn Centre, 2 Friars Close, Larkshall Road, Chingford, E4 6UN Email: Maxine.daniels@bartshealth.nhs.uk **Telephone:** 020 8535 6590	Barts Health NHS NHS Trust KING'S College LONDON University of London UNIVERSITY OF OXFORD

Chingford 1000 Women Study: Consent Form

		initial
1	I confirm that I have read, understood and have had time to consider the Patient Information Sheet (Version 2.0, dated 23 April 2013) and have been given a copy to keep. I have had the opportunity to ask questions about this project.	initial
2	I understand that my participation is voluntary and that I am free at any time to withdraw, without giving any reason, without my medical care or legal rights being affected.	initial
3	I agree that the Chingford team can collect and store information, including x-rays and photographs of my hands and feet, for research. I understand that this information may be viewed by regulatory bodies.	initial
4	I agree to give samples of blood and urine as detailed in the Patient Information Sheet.	initial
5	I agree to take part in the long term follow-up.	initial
6	I understand results from research tests on my samples might be medically important to me or my family. I agree to my GP being informed of my participation in the study and that relevant experimental findings can be discussed with them.	initial
7	I agree that the sample (s) I have given and the information gathered about me can be stored for use in future projects, subject to ethical approval, which may include genetic studies as described in the Patient Information Sheet. I understand that some of these projects may be carried out by researchers working abroad or for commercial companies. If a commercial product were developed as a result of this study I will not profit financially from such a product.	initial
8	I agree that the sample (s) of blood and urine I have given and the information gathered about me can be stored by the Oxford Musculoskeletal Biobank (OMB) in an anonymised format for the duration of the study.	initial
9	Once the study is complete, I agree to gift the samples, and the information gathered about me, to the Oxford Musculoskeletal Biobank (OMB) for possible future research projects. **Please circle: Yes / No**	initial
10	I have been informed of, and I agree to take part in, the Biomechanical Foot Assessment at the Gait Analysis Laboratory, University of East London. I agree to make my own arrangements for travel to the laboratory and participate in the additional foot research appointment. **Please circle: Yes / No**	initial

Name of participant	Signature	Date
I have discussed the study with this participant who has agreed to give informed consent.		
Name of witness	Signature	Date

Consent forms: Original to Oxford Site File, Copy to Participant, Medical Records, Silverthorne Medical Centre Site File and UEL.

Appendix 6 Study protocol for study

Recruitment	Participants who were; deceased, too unwell to attend or unable to attend for other reasons were excluded from the study.
Recruitment	Participants deemed suitable for the study invited to attend and an appointment booked to attend clinic.
Recruitment	Participants sent information sheets regarding the study.
Recruitment/ Consent	Participants seen by research assistant, given a full explanation of the study and provided with the opportunity to consent to the study (See Appendix 2).
Data collection	Background demographics collected from participants by research assistant.
Consent	Participants seen by MPhil student and given full explanation of assessments that will take place. Assessments begun following implied consent.
Data collection	Participants seen by MPhil student for foot assessments.
Data collection	Participants seen by phlebotomist & given questionnaires to complete with the option of completing them in clinic or from home & returning them by post.
Data collection	Participants seen on the same day or following their clinical appointment at SMC for foot x-rays at the Stratford Inhealth NHS site or Holly House Private Hospital.
Data collection	X-ray report from radiologist sent to research assistant at SMC & CD-ROMs of radiographic images sent by secure post to MPhil student at University of
Data analysis	Foot x-rays reviewed using the LFA by MPhil student alongside other collected variables.

Appendix 7 Ethical approval for C1000W study

NHS
Health Research Authority

NRES Committee South Central - Oxford A
Bristol Research Ethics Committee Centre
Whitefriars
Level 3 Block B
Lewins Mead
Bristol
BS1 2NT

Telephone: 0117 342 1331
Facsimile: 0117 342 0445

02 May 2013

Professor Nigel Kim Arden
1.Professor of Rheumatology and Consultant Rheumatologist; Director of Musculoskeletal Epidemiology and BioBank Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, Botnar
University of Oxford; University Hospitals Southampton NHS Trust
Botnar Research Centre, Nuffield Orthopaedic Centre,
Windmill Road
Oxford
OX3 7LD

Dear Professor Arden

Study title:	**The Chingford Study is an ongoing longitudinal study of musculoskeletal disease in the general population. The creation of the Chingford Cohort resource includes the ongoing maintenance of data, sample collection and analysis.**
REC reference:	**13/SC/0156**
IRAS project ID:	**84131**

Thank you for your letter of 01 May 2013, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chair.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Ethical review of research sites

NHS sites

Appendix 8 MFPDI

Study Number:_____ Date Completed:__/___/____ (DD/MM/YYYY)

Section 5: Foot Symptoms

Foot symptoms Part 1.

24. Below are some statements about problems people have because of pain in their feet. For each statement indicate if this has applied to you during the past month. If so, was this only on some days or on most or every day in the past month?

The Manchester Foot Pain and Disability Index a.garrow@salford.ac.uk

Garrow AP, Papageorgiou AC, Silman AJ, Thomas E, Jayson MI, Macfarlane GJ. Development and validation of a questionnaire to assess disabling foot pain. Pain Mar; 85(1-2):107-13 2000

Below are some statements about problems people have **because of pain in their feet.**

For each statement indicate if this has applied to you **during the past month.** If so, was this only on some days or on most or every day in the past month?

PLEASE TICK A BOX FOR EACH STATEMENT.

	During the past month this has applied to me		
Because of pain in my feet:	None of the time	On some days	On most/ every day(s)
I avoid walking outside at all	☐	☐	☐
I avoid walking long distances	☐	☐	☐
I don't walk in a normal way	☐	☐	☐
I walk slowly	☐	☐	☐
I have to stop and rest my feet	☐	☐	☐
I avoid hard or rough surfaces when possible	☐	☐	☐
I avoid standing for a long time	☐	☐	☐
I catch the bus or use the car more often	☐	☐	☐
I need help with housework/shopping	☐	☐	☐
I get irritable when my feet hurt	☐	☐	☐
Because of pain in my feet:			
I feel self-conscious about my feet	☐	☐	☐
I feel self-conscious about the shoes I have to wear	☐	☐	☐
I still do everything but with more pain and discomfort	☐	☐	☐
I have constant pain in my feet	☐	☐	☐
My feet are worse in the morning	☐	☐	☐
My feet are more painful in the evening	☐	☐	☐
I get shooting pains in my feet	☐	☐	☐

Office Use Only

Scoring

0=None of the time
1=On some days
2=On most/everyday(s)
50=Not Applicable
999=Missing

Sub-scales

Functional - Items 1-10
Range 0-20

Personal Appearance
Items 11-12
Range 0-4

Pain – Items 13-17
Range 0-10

Work/Leisure
Items 18-19
Range 0-100

Appendix 9 Possible bias introduced into research

Area of research	Possible bias	Summary of definition	Relevance to study	Impact on results
Recruitment	**Selection bias** (Bowling 2009, p.175)	Where characteristics from the sample differ with those of the general population.	In terms of the recruitment at baseline, differences between selected and non-selected groups for the study should be minimal for 1989. No statistical significance was shown through work at the beginning of the chapter. *Also see 'Cohort effect bias'*	If any bias existed, the prevalence of co-morbidities in the non-selected group may result in the under-estimation of foot osteoarthritis. This is due to the possible exclusion of participants likely to have osteoarthritis and potentially with more serious cases.
	Memory (recall) bias (Bowling 2009, p.174)	Difficulty in recalling events in the past.	Questions referred to 'ever' having pain. Such experiences may have been forgotten by participants. Participants are also within an older age range where memory may be an issue.	If memory recall did impact the responses of the participants, there will be under-estimation of foot pain (where self-assessed foot pain is considered).
	Acquiescence response set (Bowling 2009, p.172)	More often agree with a statement than disagree and thus being passive in their responses.	Questionnaires were in total 44 pages in length. There may have been a point where participants became fatigued in answering questions.	Participants may have tended to answer positively (if majority of the true answers were positive) or negatively (where the majority are true). This will either result in the over-estimation or under-estimation of pain respectively.

Participant responses	**Mood bias** (Bowling 2009, p.173)	People who are not in good form or in 'low spirits' who underestimate health status, support, social activity levels and ability to function.	The temperament, attitude and mood of participants cannot be controlled during the study due to the circumstantial nature and on occasion the mental health of participants. These could have been influential in the answering of the questionnaires.	A positive mood may result in participants' responses being negative to the questions (i.e. No pain, no medical problems etc.). A negative mood may result in participants' responses being positive to the questions (i.e. No pain, no medical problems etc.). Negative responses will result in under-estimation of foot pain where positive responses will result in over-estimation of pain.
	Non-response bias (Bowling 2009, p.173)	Answers are different in those who responded to those who did not respond or who did not participate in the study.	Two relevant groups existed in the study. Those opting out of their involvement in the year '23' clinical visit altogether and those opting out of their involvement in the x-ray.	Those opting out of the year '23' study altogether may not have attended as they were too ill, or their symptoms were too severe to attend or had mental health problems. This would most likely mean that the severe cases of osteoarthritis may be excluded from the study. Where mental health illness exists, this may impact the experience of pain. These 'opt-out' participants could under-estimate prevalence of

				foot osteoarthritis and/or foot pain respectively. 'Opt-out' participants for the x-ray may have been opting out based on having had recent exposure to medical radiation, if this is the case, this could result in further under-estimation of foot osteoarthritis. This was analysed in study 2 to
Observer recording	**Observer bias** (Bowling 2009, p.173)	Disparity between the 'true' and 'recorded' results of a study due to variation in observation and influences from perception.	Evaluation of foot osteoarthritis involved a level of subjectivity despite being minimised with a revised technique (technique 2). However, this means that there was opportunity for unreliable results.	Over-estimation or under-estimation could have occurred in this instance.
	Response order-effect bias (Villars 2008 p751)	This is based on the order of questioning which can influence responses given by participants.	Pain questions were all in the penultimate section. This is preferable as first and last sections are often more memorised. However, the length of questionnaires may mean that people who give up before the end do not answer these questions.	Order bias is less likely to exist due to the placement of questionnaires. Difficulty may arise where data are missing.

Participant characteristics	**Cohort effect bias** (Bowling 2009, p.222)	Where participants have been recruited in a longitudinal study, recruitment areas are open to social, economic, cultural and demographic change with those moving into and out of the area over time. This can differ substantially from the group recruited at baseline meaning the study is no longer representative of that area.	The study in 1989 was representative of participants in the area of Chingford being 98% Caucasian and lower to middle class. Trends would suggest that political changes in the Greater London area have increased the ethnic diversity and reduced the level of socioeconomic class. The study was at baseline based in geographical region of Essex. This is now the region of Greater London.	Results will be limited to Caucasian British women with little scope to generalise findings to the general population of Chingford, London or Essex.
	Survival bias Delgado-Rodriguez and Llorca (2004)	This is where exclusion of participants with a certain characteristic are excluded. Bias occurs where the characteristic is related to increased mortality rate.	The primary focus of this thesis was with pain, of which, persistent pain is linked to increased mortality among older women in a five-year period (Shega et al. 2013). Specific association with the feet is unknown.	Participant who previously had pain experiences are more likely to have passed away. As a result, pain may be underestimated within prevalence work relating to pain. This is accepted as a limitation.
	Length bias Delgado-Rodriguez and Llorca (2004)	The participants within the sample are often (where it is an older group) healthier and have survived longer. This means differences exist in the quality of	The highest mortality rate (n=223) occurred between the previous (Year 20) and last follow-up visits (year '23'). As an aging cohort, it is possible that the weakest and sick are	Severe foot osteoarthritis and foot osteoarthritis where co-morbidities exist, may not be captured within the study population due to the passing away of these participants. This could

		life compared with those who die earlier.	passing away at a higher rate than healthy participants.	influence the results to show a lower prevalence of foot osteoarthritis and of pain (Shega et al. 2013).
	Neyman bias Delgado-Rodriguez and Llorca (2004)	Where survivors make up the sample, and exposure is related to the outcome or prognostic factors.	Participants in the study are women and older aged. Both are exposures which are prognostic determinants.	Prevalence of foot osteoarthritis and of foot pain will be over-estimated. However, this is recognised and is why Year 6 x-rays are also included for prevalence work for exploration in Chapter 6. As the design of the study is for the inclusion of women and exclusion of men, the recommendation has been given for future work aims to consider both genders.

Appendix 10 Manchester Foot Pain and Disability Index 17 (MFPDI)

Response frequencies of Australian and London based populations (NWAHS (W) N=135; NWASHS (Yrs) N=57; C1000W N=118) (Menz et al. 2011)

Question: ***'Because of pain in my feet…'***	**Cohort**	**None of the time (n)**	**On some days (n)**	**On most days (n)**
I avoid walking outside at all	**NWAHS (W)[¥]**	75.6% (102)	17.8% (24)	6.7% (9)
	NWAHS (Yrs)[‡]	75.4% (43)	14.0% (8)	10.5% (6)
	C1000WS	89.8% (106)	8.5% (10)	1.7% (2)
I avoid walking long distances	**NWAHS (W)**	31.3% (42)	31.3% (42)	37.8% (51)
	NWAHS (Yrs)	28.1% (16)	19.3% (11)	52.6% (30)
	C1000WS	44.1% (52)	43.2% (51)	12.7% (15)
I don't walk in a normal way	**NWAHS (W)**	41.0% (55)	32.1% (43)	26.9% (36)
	NWAHS (Yrs)	57.9% (33)	15.8% (9)	26.3% (15)
	C1000WS	66.9% (79)	20.3% (24)	12.7% (15)
I walk slowly	**NWAHS (W)**	35.1% (47)	32.8% (44)	32.1% (43)
	NWAHS (Yrs)	28.6% (16)	17.9% (10)	53.6% (30)
	C1000WS	41.5% (49)	39.0% (46)	19.5% (23)
I have to stop and rest my feet	**NWAHS (W)**	43.0% (58)	25.6% (48)	21.5% (29)
	NWAHS (Yrs)	52.6% (30)	12.3% (7)	35.1% (20)
	C1000WS	73.7% (87)	18.6% (22)	7.6% (9)
I avoid hard or rough surfaces when possible	**NWAHS (W)**	32.1% (43)	20.1% (27)	47.8% (64)
	NWAHS (Yrs)	28.1% (16)	8.8% (5)	63.2% (36)
	C1000WS	40.7% (48)	40.7% (48)	18.6% (22)
I avoid standing for a long time	**NWAHS (W)**	19.3% (26)	27.4% (37)	53.3% (72)
	NWAHS (Yrs)	21.1% (12)	12.3% (7)	66.7% (38)
	C1000WS	32.2% (38)	41.5% (49)	26.3% (31)
I catch the bus or use the car more often	**NWAHS (W)**	44.8% (60)	12.7% (17)	42.5% (57)
	NWAHS (Yrs)	43.9% (25)	8.8% (5)	47.4% (27)
	C1000WS	30.5% (36)	37.3% (44)	32.2% (38)
I need help with housework/shopping	**NWAHS (W)**	77.8% (105)	13.3% (18)	8.9% (12)
	NWAHS (Yrs)	75.4% (43)	15.8% (9)	8.8% (5)
	C1000WS	75.4% (89)	13.6% (16)	11.0% (13)
I get irritable when my feet hurt	**NWAHS (W)**	34.8% (47)	42.2% (57)	23.0% (31)
	NWAHS (Yrs)	47.4% (27)	31.6% (18)	21.1% (12)
	C1000WS	66.9% (79)	29.7% (35)	3.4% (4)
I feel self-conscious about my feet	**NWAHS (W)**	63.7% (86)	14.8% (20)	21.5% (29)
	NWAHS (Yrs)	68.4% (39)	12.3% (7)	19.3% (11)
	C1000WS	74.6% (88)	15.3% (18)	10.2% (12)
I feel self-conscious about the shoes I have to wear	**NWAHS (W)**	76.1% (67)	19.3% (26)	19.3% (26)
	NWAHS (Yrs)	66.7% (38)	22.8% (13)	10.5% (6)
	C1000WS	71.2% (84)	20.3% (24)	8.5% (10)
I still do everything but with more pain and discomfort	**NWAHS (W)**	10.4% (14)	33.6 (45)	56.0% (75)
	NWAHS (Yrs)	12.5% (7)	23.2% (13)	64.3% (36)
	C1000WS	43.2% (51)	40.7% (48)	16.1% (19)
I have constant pain in my feet	**NWAHS (W)**	28.1% (38)	30.4% (41)	41.5% (56)
	NWAHS (Yrs)	28.1% (16)	26.3% (15)	45.6% (26)
	C1000WS	57.6% (68)	29.7% (35)	12.7% (15)
My feet are worse in the morning	**NWAHS (W)**	50.8% (67)	20.5% (27)	28.8% (38)
	NWAHS (Yrs)	66.1% (37)	7.1% (4)	26.8% (15)
	C1000WS	71.2% (84)	21.2% (25)	7.6% (9)

My feet are more painful in the evening	**NWAHS (W)**	25.4% (34)	32.8% (44)	41.8% (56)
	NWAHS (Yrs)	37.5% (21)	25.0% (14)	37.5% (21)
	C1000WS	63.6% (75)	27.1% (32)	9.3% (11)
I get shooting pains in my feet	**NWAHS (W)**	39.3% (53)	43.0% (58)	17.8% (24)
	NWAHS (Yrs)	52.6% (30)	33.3% (19)	14.0% (8)
	C1000WS	72.0% (85)	22.9% (27)	5.1% (6)

**Participants were all women who had answered positively to having pain 'most days' in the last month (NWAHS N=135; C1000W N=118)*

[¥]Participants were stratified according to gender, data for women are presented in the table

[‡]Participants were stratified according to age, data for participants aged 71 to 90 years are presented in the table.

Appendix 11 Prevalence of osteoarthritis stratified according to grading in the dorsoplantar view

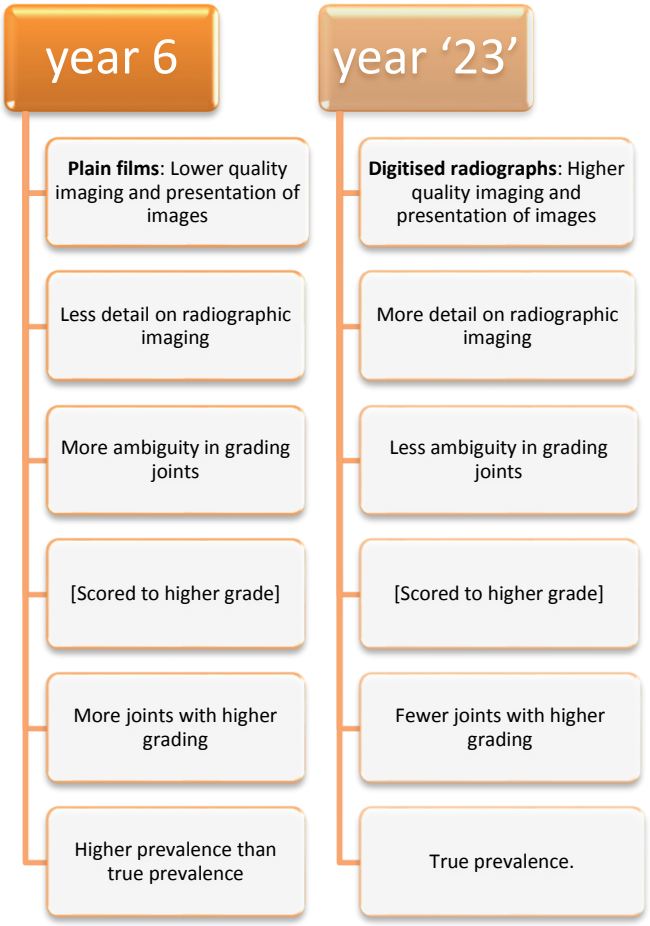
			0			**1**			**2**			**3**			**Ungradable**
Foot	Joints	RG sign	LFA method	Adjusted	Ungrad-able excl.	LFA method	Adjusted	Ungrad-able excl.	LFA method	Adjusted	Ungrad-able excl.	LFA method	Adjusted	Ungrad-able excl.	Ungradable excluded
Left	1st MTPJ	OP	85 (39)	64 (29.4)	85 (39)	78 (35.8)	83 (38.1)	77 (35.3)	36 (16.5)	48 (22.0)	35 (16.1)	19 (8.7)	23 (10.6)	19 (8.7)	2 (0.9)
		JSN	60 (27.5)	51 (23.4)	60 (27.5)	130 (59.6)	122 (56.0)	129 (59.2)	12 (5.5)	28 (12.8)	12 (5.5)	16 (7.3)	17 (7.8)	16 (7.3)	1 (0.5)
	1st CMJ	OP	189 (86.7)	175 (80.3)	166 (76.1)	26 (11.9)	39 (17.9)	21 (9.6)	3 (1.4)	4 (1.8)	3 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	28 (12.8)
		JSN	36 (16.5)	25 (11.5)	34 (15.6)	85 (39.0)	59 (27.1)	83 (38.1)	87 (39.1)	113 (51.8)	82 (37.6)	10 (4.6)	21 (9.6)	9 (4.1)	10 (4.6)
	2nd CMJ	OP	200 (91.7)	199 (91.3)	105 (48.2)	15 (6.9)	15 (6.9)	8 (3.7)	3 (1.4)	4 (1.8)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	104 (47.7)
		JSN	31 (14.2)	29 (13.3)	26 (11.9)	79 (36.2)	69 (31.7)	44 (20.2)	104 (47.7)	113 (51.8)	44 (20.2)	4 (1.4)	7 (3.2)	0 (0.0)	104 (47.7)
	N1stCJ	OP	207 (95.0)	195 (89.4)	194 (89.0)	9 (4.1)	21 (9.6)	8 (3.7)	1 (0.5)	1 (0.5)	1 (0.5)	1 (0.5)	1 (0.5)	1 0.5)	14 6.4)
		JSN	19 (8.7)	14 (6.4)	19 (8.7)	159 (72.9)	54 (24.8)	152 (69.7)	36 (16.5)	145 (66.5)	35 (16.1)	4 (1.4)	5 (2.3)	3 (1.4)	9 (4.1)
	TNJ	OP													
		JSN	44 (20.2)	31 (14.2)	44 (20.2)	158 (72.5)	137 (62.8)	158 (72.5)	15 (6.9)	48 (22.0)	15 (6.9)	1 (0.5)	2 (0.9)	1 (0.5)	0 (0.0)
Right	1st MTPJ	OP	73 (33.5)	54 (24.8)	73 (33.5)	76 (34.9)	79 (36.2)	76 (34.9)	45 (20.6)	57 (26.1)	45 (20.6)	24 (11.0)	28 (12.8)	22 (10.1)	2 (0.9)
		JSN	57 (26.1)	38 (17.4)	57 (26.1)	131 (60.1)	123 (56.4)	131 (60.1)	17 (7.8)	40 (18.3)	17 (7.8)	13 (6.0)	17 (7.8)	12 (5.5)	1 (0.5)
	1st CMJ	OP	188 (86.2)	169 (77.5)	166 (76.1)	29 (13.3)	48 (22.0)	25 (11.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.5)	1 (0.5)	26 (11.9)
		JSN	31 (14.2)	21 (9.6)	31 (14.2)	84 (38.5)	58 (26.6)	82 (37.6)	89 (40.8)	113 (51.8)	86 (39.4)	14 (6.4)	26 (11.9)	13 (6.0)	6 (2.8)
	2nd CMJ	OP	211 (96.8)	207 (95.0)	108 (49.5)	5 (2.3)	9 (4.1)	3 (1.4)	2 (0.9)	2 (0.9)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	106 (48.6)
		JSN	32 (14.7)	27 (12.4)	28 (12.8)	83 (38.1)	72 (33.0)	51 (23.4)	99 (45.4)	111 (50.9)	40 (18.3)	4 (1.8)	8 (3.7)	0 (0.0)	99 (45.4)
	N1stCJ	OP	193 (88.5)	177 (81.2)	183 (83.9)	23 (10.6)	37 (17.0)	19 (8.7)	1 (0.5)	3 (1.4)	1 (0.5)	1 (0.5)	1 (0.5)	1 (0.5)	14 (6.4)
		JSN	15 (6.9)	10 (4.6)	14 (6.4)	165 (75.7)	51 (23.4)	161 (73.9)	35 (16.1)	150 (68.8)	33 (15.1)	3 (1.4)	7 (3.2)	2 (0.9)	8 (3.7)
	TNJ	OP													
		JSN	28 (12.8)	17 (7.8)	28 (12.8)	173 (79.4)	146 (67.0)	173 (79.4)	16 (7.3)	53 (24.3)	16 (7.3)	1 (0.5)	2 (0.9)	1 (0.5)	0 (0.0)

Appendix 12 Prevalence of osteoarthritis stratified according to grading in the lateral view

			0			**1**			**2**			**3**			**Ungradable**
Foot	Joints	RG sign	LFA method	Adjusted	Ungrad-able excl.	LFA method	Adjusted	Ungrad-able excl.	LFA method	Adjusted	Ungrad-able excl.	LFA method	Adjusted	Ungrad-able excl.	Ungradable excluded
Left	1st MTPJ	OP	154 (70.6)	151 (69.3)	139 (63.8)	44 (20.2)	43 (19.7)	37 (17.0)	15 (6.9)	19 (8.7)	11 (5.0)	5 (2.3)	5 (2.3)	5 (2.3)	26 (11.9)
		JSN	78 (35.8)	73 (33.5)	29 (13.3)	99 (45.4)	103 (47.2)	31 (14.2)	25 (11.5)	26 (11.9)	9 (4.1)	16 (7.3)	16 (7.3)	5 (2.3)	144 (66.1)
	1st CMJ	OP	200 (91.7)	193 (88.5)	188 (86.2)	13 (6.0)	20 (9.2)	10 (4.6)	4 (1.8)	4 (1.8)	3 (1.4)	1 (0.5)	1 (0.5)	1 (0.5)	16 (7.3)
		JSN	61 (28.0)	45 (20.6)	59 (27.1)	137 (62.8)	141 (64.7)	129 (59.2)	18 (8.3)	29 (13.3)	15 (6.9)	2 (0.9)	3 (1.4)	1 (0.5)	14 (6.4)
	2nd CMJ	OP	179 (82.1)	173 (79.4)	115 (52.8)	20 (9.2)	24 (11.0)	10 (4.6)	14 (6.4)	16 (7.3)	7 (3.2)	5 (2.3)	5 (2.3)	3 (1.4)	83 (38.1)
		JSN	7 (3.2)	7 (3.2)	3 (1.4)	89 (40.8)	75 (34.4)	23 (10.6)	109 (50.0)	118 (54.1)	30 (13.8)	13 (6.0)	18 (8.3)	5 (2.3)	157 (72.0)
	N1stCJ	OP	169 (77.5)	165 (75.7)	141 (64.7)	32 (14.7)	31 (14.2)	24 (11.0)	15 (6.9)	20 (9.2)	10 (4.6)	2 (0.9)	2 (0.9)	2 (0.9)	41 (18.8)
		JSN	79 (36.2)	70 (32.1)	51 (23.4)	128 (58.7)	129 (59.2)	69 (31.7)	9 (4.1)	17 (7.8)	3 (1.4)	2 (0.9)	2 (0.9)	2 (0.9)	93 (42.7)
	TNJ	OP	146 (67.0)	120 (55.0)	143 (65.6)	48 (22.0)	71 (32.6)	46 (21.1)	22 (10.1)	20 (9.2)	19 (8.7)	2 (0.9)	7 (3.2)	2 (0.9)	8 (3.7)
		JSN	48 (22.0)	35 (16.1)	46 (21.1)	142 (65.1)	135 (61.9)	141 (64.7)	26 (11.9)	46 (21.1)	26 (11.9)	2 (0.9)	2 (0.9)	2 (0.9)	3 (1.4)
Right	1st MTPJ	OP	137 (62.8)	132 (60.6)	121 (55.5)	49 (22.5)	48 (22.0)	38 (17.4)	24 (11.0)	29 (13.3)	20 (9.2)	8 (3.7)	9 (4.1)	7 (3.2)	32 (14.7)
		JSN	87 (39.9)	83 (38.1)	44 (20.2)	88 (40.4)	92 (42.2)	28 (12.8)	31 (14.2)	30 (13.8)	4 (1.8)	12 (5.5)	13 (6.0)	2 (0.9)	140 (64.2)
	1st CMJ	OP	195 (89.4)	188 (86.2)	187 (85.5)	14 (6.4)	20 (10.1)	13 (6.0)	7 (3.2)	8 (3.7)	4 (1.8)	2 (0.9)	2 (0.9)	1 (0.5)	13 (6.0)
		JSN	71 (32.6)	50 (22.9)	70 (32.1)	129 (59.2)	140 (64.2)	121 (55.5)	17 (7.8)	27 (12.4)	14 (6.4)	1 (0.5)	1 (0.5)	1 (0.5)	12 (5.5)
	2nd CMJ	OP	177 (81.2)	171 (78.4)	110 (50.5)	22 (10.1)	25 (11.5)	10 (4.6)	10 (4.6)	11 (5.0)	7 (3.2)	9 (4.1)	11 (5.0)	4 (1.8)	87 (39.9)
		JSN	13 (6.0)	11 (5.0)	3 (1.4)	84 (38.5)	78 (35.8)	24 (11.0)	106 (48.6)	107 (49.1)	26 (11.9)	15 (6.9)	22 (10.1)	2 (0.5)	163 (74.8)
	N1stCJ	OP	170 (78.0)	163 (74.8)	137 (62.8)	35 (16.1)	38 (17.4)	26 (11.9)	11 (5.0)	13 (6.0)	7 (3.2)	2 (0.9)	4 (1.8)	2 (0.9)	46 (21.1)
		JSN	101 (46.3)	91 (41.7)	62 (28.4)	104 (47.7)	108 (49.5)	53 (24.3)	11 (5.0)	17 (7.8)	5 (2.3)	2 (0.9)	2 (0.9)	1 (0.5)	97 (44.5)
	TNJ	OP	128 (58.7)	90 (41.3)	126 (57.8)	71 (32.6)	102 (46.8)	69 (31.7)	16 (7.3)	21 (9.6)	15 (6.9)	3 (1.4)	5 (2.3)	3 (1.4)	5 (2.3)

		JSN	68 (31.2)	47 (21.6)	66 (30.3)	129 (59.2)	132 (60.6)	129 (59.2)	19 (8.7)	37 (17.0)	19 (8.7)	2 (0.9)	2 (0.9)	2 (0.9)	2 (0.9)

Appendix 13 Impact on results from the limitation of differing x-ray methods



Appendix 14 IMFAA incorporated into Chingford questionnaires

Study Number:_____ Date Completed____/____/_____(DD/MM/YYYY)
25.

A.	Swollen (tender) joint			
Observation	Left		Right	
1st MTPJ	Yes	No	Yes	No
Presence of pain*	Yes	No	Yes	No
2nd MTPJ	Yes	No	Yes	No
Presence of pain*	Yes	No	Yes	No
3rd MTPJ	Yes	No	Yes	No
Presence of pain*	Yes	No	Yes	No
4th MTPJ	Yes	No	Yes	No
Presence of pain*	Yes	No	Yes	No
5th MTPJ	Yes	No	Yes	No
Presence of pain*	Yes	No	Yes	No
1st CMJ*	Yes	No	Yes	No
Presence of pain*	Yes	No	Yes	No
2nd CMJ*	Yes	No	Yes	No
Presence of pain*	Yes	No	Yes	No
1st CNJ (N1stCNJ)*	Yes	No	Yes	No
Presence of pain*	Yes	No	Yes	No
Midfoot	Yes	No	Yes	No
Presence of pain*	Yes	No	Yes	No
STJ	Yes	No	Yes	No
Presence of pain*	Yes	No	Yes	No
Ankle	Yes	No	Yes	No
Presence of pain*	Yes	No	Yes	No

B.	Skin/nail changes and/or lesions	
Observation	Left	Right
Skin changes:		
Nail changes:		

C.	General foot morphology			
Observation	Left		Right	
Abnormality	Normal	Abnormal	Normal	Abnormal
Symmetrical	Yes / No			

D.	Hallux valgus presence			
Observation	Left		Right	
	Yes	No	Yes	No

E.	Lesser toe deformities					
Observation	Left			Right		
		How many			How many	
Hammer	Yes		No	Yes		No
Mallet	Yes		No	Yes		No
Retracted	Yes		No	Yes		No
Clawed	Yes		No	Yes		No

Study Number:_____ Date Completed____/____/_____(DD/MM/YYYY)

F.	Achilles Tendon				
Palpation	Site	Left		Right	
Tender	T-A Junction	Yes	No	Yes	No
	Mid Tendon	Yes	No	Yes	No
	Enthesis	Yes	No	Yes	No
Thickened	Full	Yes	No	Yes	No

G.	Proximal plantarfascia insertion			
Palpation	Left		Right	
Tender	Yes	No	Yes	No

H.	Joint Assessment							
Range of Motion	Left				Right			
Ankle Joint Dorsiflexion with knee extended	Hyper-mobile	Normal	Limited	Fixed	Hyper-mobile	Normal	Limited	Fixed
Ankle Joint Dorsiflexion with knee flexed	Hyper-mobile	Normal	Limited	Fixed	Hyper-mobile	Normal	Limited	Fixed
Rearfoot inversion/eversion	Hyper-mobile	Normal	Limited	Fixed	Hyper-mobile	Normal	Limited	Fixed
Midfoot /midtarsal Joint	Hyper-mobile	Normal	Limited	Fixed	Hyper-mobile	Normal	Limited	Fixed
1st MTPJ	Hyper-mobile	Normal	Limited	Fixed	Hyper-mobile	Normal	Limited	Fixed
Metatarsal phalangeal joints	Hyper-mobile	Normal	Limited	Fixed	Hyper-mobile	Normal	Limited	Fixed
1st CMJ bony prominence*	Yes		No		Yes		No	
2nd CMJ bony prominence*	Yes		No		Yes		No	
1st CNJ (N1stCNJ) bony prominence*	Yes		No		Yes		No	

I.	Muscle Tests									
Mark as appropriate	Left					Right				
Gastrocnemius/Soleus (MRC scale)	1	2	3	4	5	1	2	3	4	5
Single limb heel raise (tibialis posterior)	Able	Limited	Unable			Able	Limited	Unable		

J.	Alignment					
Mark as appropriate	Left			Right		
Rearfoot to leg (relaxed stance)	Inverted	Linear	Everted	Inverted	Linear	Everted

Study Number:_____ Date Completed___/___/_____(DD/MM/YYYY)

Foot Posture Index (FPI)	Left					Right				
Talar head palpation	-2	-1	0	+1	+2	-2	-1	0	+1	+2
Curves above and below malleoli	-2	-1	0	+1	+2	-2	-1	0	+1	+2
Calcaneal inversion/eversion	-2	-1	0	+1	+2	-2	-1	0	+1	+2
Talo-navicular prominence	-2	-1	0	+1	+2	-2	-1	0	+1	+2
Medial arch height	-2	-1	0	+1	+2	-2	-1	0	+1	+2
Forefoot abduction/adduction	-2	-1	0	+1	+2	-2	-1	0	+1	+2
Total										

L.	Leg Length	
Indirect assessment	Left	Right
	ASIS-MM (mm):	ASIS-MM (mm):

M.	Footwear							
Shoe Type with % worn in average week	Trainer	%	Boot	%	Oxford/ lace	%	Court	%
	Slip-on	%	Sandal	%	Be spoke	%	Slipper	%
Heel Height in an average week.	Low (0-2.5 cm)		Medium (2.6-5 cm)		High (>5 cm)			

N.	Gait parameters	
Walking aid	Yes	No
Lower Limb Asymmetry	Yes	No
Anatlgic Gait	Yes	No
Ataxic Gait	Yes	No
Festinating Gait	Yes	No
Hemiplegic Gait	Yes	No
Spastic Gait	Yes	No
10m walk time	.....seconds	

*Assessments highlighted in green and orange are in addition to the Foot Assessment Tool questions.**26.Other comments:**

A. Dominant Foot:

.....

B. Foot Ulceration:

.....

C. Foot Orthoses:

.....

D. Other:

.....

E. *Further actions required?*

Referral for Biomechanical Assessment: Yes / No

Referral to Orthotist: Yes / No

Referral to Consultant / GP: Yes / No

Referral to Podiatrist: Yes / No

Appendix 15 La Trobe Foot Atlas limitations

Atlas limitation	Reason for limitation	Type of limitation
No narrative guide to images	No narrative means there is a reliance on either experience of the user in appreciating or describing radiographs or the development of skills through recognition of graduated observable changes among atlas images for each osteoarthritic characteristic (OP or JSN).	Atlas: Guidance Experience of observer
Limited number of joints assessed	There are 32 joints in the foot of which only 5 are evaluated using the LFA.	Atlas: Scope or extent of evaluation
Multiplanar functionality of joints	This may affect the ability to standardise x-rays and ensure repeatability particularly in JSN. JSN in the hips and knees have been identified as significant factors affecting radiographic JSN (Leach et al. 1970).	Atlas: Physiological
No consideration of foot deformity (HAV)	Visual disparity results in inappropriate comparisons between the LFA and images reviewed	Atlas: Pathophysiological Limitation of atlas
Appearance of images from LFA can be confusing	Overlap of bones at joints can be confusing	Experience of observer
Pathological uncertainty among LFA images.	Uncertainty over what constitutes an osteophyte within a joint i.e. Talo-navicular joint (TNJ)	Atlas: Guidance Experience of observer
Atlas duplicate images	Duplicate images for the same joint were on occasions used to demonstrate both JSN and OPs. This can be misguiding due to the influence of other characteristics in osteoarthritis or cognitive bias and result in a divergence from the true observations	Atlas: Usability Experience of observer
TNJ excludes OP assessment without explanation	No explanation is provided for the exclusion of this osteoarthritis characteristic for this specific joint.	Atlas: Guidance
Lack of joint assessments in the mid-tarsal area	Joints do not consider any of the lateral mid-tarsal joints. The authors do not provide a justification for this	Atlas: Bias towards joint areas

Racial generalisability	Racial variation has not been disclosed by the authors of the atlas and therefore the generalisability is unknown. However, it is known that the feet exhibit different phenotypical characteristics between races (Golightly et al. 2012)	Atlas: Consideration of categorical phenotypes
No consideration of static foot posture	This may affect the ability to standardise x-rays and ensure repeatability particularly in JSN	Atlas: Physiological function
Disparity of grading between K&L and LFA atlases	K&L incorporate a 0-4 scale compared to a 0-3 scale used in the LFA thus reducing the scale and decreasing the variability in disease gradation (see table 1).	Atlas: Structured grading system
Disparity in grading definitions	Definitions between atlases differ substantially and LFA provides independent definitions between OPs & JSN (see table 1).	Atlas: Usability

**Areas limited by the experience of the observer*
[¥]Observer are highlighted in green

Appendix 16 Core measures of data collection for the benefit of future research

Core measure	Source	Reference	Justification
Medical History	N/A	N/A	These variables will benefit more in-depth investigation into pharmacological impact in foot osteoarthritis and pain and lower limb joint surgeries impacting the foot osteoarthritis (Arden 2006).
Medications			
Musculoskeletal foot status	IMFAA	Gates et al. (2013)	The (pre-publication) research from the biomechanical arm of the ELFOAB project found biomechanical markers specific to osteoarthritis, the additional variables are a benefit to the development of this work.
Standing foot posture			Limb dominance was collected with the intention to consider co-existing prevalence with osteoarthritis to support the discussion on prevalence of osteoarthritis.
Foot Posture			Foot posture was an important population characteristic to present in the study to provide an understanding of foot related characteristics.
Foot swelling & tenderness			Joint swelling and tenderness bare relevance to the clinical symptoms of osteoarthritis (Arden 2006).
Footwear	Footwear assessment tool	Barton et al. (2009)	Effects of footwear on joint loading and osteoarthritis are important are an important consideration for the Chingford 1000 women considering footwear trends have been observed (Bowen et al. 2016).
Weight-bearing photographs	N/A	N/A	Photographs were taken for both feet for each participant for purposes of presentation and recording foot morphology as with previous research in foot osteoarthritis (Roddy et al. 2011).
10m timed 'get-up and go' test	The Copenhagen Psychological Questionnaire	Kristensen et al. (2005)	There is a known association between timed get up and go test and knee osteoarthritis. This bares relevance to foot osteoarthritis and would be important research regardless of outcome.
Hand nodes	(Unnamed) GOAL postal survey	O'Reilly et al. (1999)	Hand nodes have a known association with generalised osteoarthritis, and this is an important consideration with foot osteoarthritis (Kellgren and Moore 1952).

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